CHAPTER 2

Blueprint for a software-based decision-support system for countering anthelmintic resistance at farm level

2.1 Introduction

As often occurrs with new technology, the FAMACHA© system, which was devised for sustainable worm management, is only slowly being adopted by farmers. It has been suggested that an important reason for this unwillingness is due in part to the complexity of integration of the FAMACHA© method with epidemiological factors, and partially to disbelief that resistance would ever become a problem, granted the dozens of different anthelmintics on the market. Reluctance to adopt the FAMACHA© system could be a reflection of the labour effort involved, as even where labour is not expensive, farmers have many demands on their time. The alternatives to the simple drenching programmes of the past are not only more difficult to manage, but are also more labour intensive. The problem is complicated further by a progressive global shortage of persons with the necessary experience to train farmers in the new methods.

It is suggested that only decision-support software will be able optimally to integrate the range of factors such as rainfall, temperature, host age and reproductive status, pasture type, pasture infectivity and anthelmintic formulation for sustainable worm management. The computer model being proposed is to be based almost entirely on periodic retrospective analysis of clinical data accumulating during a given worm season and is to consist almost entirely of tactical, targeted selective treatment, in contrast to conventional strategic drenching of all animals.

In 1985 Van Wyk warned that, unless anthelmintics were used more sustainably, it was possible that resistance would affect all available compounds to the extent that no effective remedies would remain for worm control. To this, Van Wyk (1990) added that while the above was regarded even by some helminthologists as alarmist, it seemed possible that resistance could escalate to include compounds from all the anthelmintic groups in individual worm populations. In 1997 the first case was reported where the total population of a worm species was resistant to compounds from all of the anthelmintic activity groups available for use against gastrointestinal nematodes in sheep and cattle at the time, namely the benzimidazoles, imidazothiazoles, macrocyclic lactones, organophosphates and the salicylanilides/substituted nitrophenols, as well as the first reported cases of resistance to nitroxynil and disophenol (Van Wyk, Malan & Randles 1997b). Although resistance was referred to as "rampant" at the time (Van Wyk, Malan & Bath 1997a), it was still borderline in the case of some of the compounds. Subsequently it has escalated continuously, recently causing Van Wyk (2006) to comment that we had entered the final phase where nothing remained on some farms with which to control worms at a level commensurate with profitable animal production.

Van Wyk *et al*. (1999) recorded some populations of *H. contortus* that were less than 40 % susceptible to all four of the compounds used in their surveys in South Africa, namely rafoxanide, albendazole, levamisole and ivermectin, to represent the four different activity groups on the market at the time. Today even moxidectin, arguably the last major compound to reach the market, is already seriously affected by resistance (Leathwick 1995; Thomaz-Soccol, De Souza, Sotomaior, Castro, Milczewski, Mocelin, Pessoa & Silva 2004; Rhodes, Leathwick, Pomroy, West, Jackson, Lawrence, Moffat & Waghorn 2006). In some cases there has been practically complete failure even when moxidectin was administered together with other compounds (Table 2.1 – C.S. Sotomaior, personal communication 2006).

TABLE 2.1 Worm populations found in a survey in Paraná State, Brazil, to be less than 80 % susceptible to moxidectin drenched either alone or together with other compounds (C. S. Sotomaior, personal communication 2006)

Worm populations	**Moxidectin**	**Moxidectin plus other***
Less than 80 % susceptible	21	6
Less than 30 % susceptible	6	0
Mean	48 %	55 %
Range	0-74 %	30-77 %

*Moxidectin and closantel and/or moxidectin and nitroxynil

While previously only marginally affected by drug resistance, the worms of cattle are following suit (Hosking, Watson & Leathwick 1996; McKenna 1996; Rhodes *et al*. 2006), leading to a warning by Waller (1997, 2003) that cattle worms had already reached levels of anthelmintic resistance similar to those at which the worms of small ruminants had been a decade earlier. Coronado, Escalona, Henriquez, Mujica & Suarez (2003) recorded total failure of ivermectin against a population of *Cooperia* sp. infection in cattle in Venezuela.

The number of resistant bovine worm populations is rising rapidly, as indicated by resistance to ivermectin on 55 % of 69 farms surveyed in Argentina (Caracostantogolo, Castaño, Cutullé, Cetrá, Lamberti, Olaechea, Ruiz, Schapiro, Martinez, Balbiani & Castro 2005).

2.2 Refugia for sustainable worm management

Parasites which escape any given control measure, for example worms on pasture when their hosts are drenched, are said to be in refugia (Martin, Le Jambre & Claxton 1981; Martin 1989; Van Wyk 2001). One of the most effective ways of obtaining relatively large numbers of worms in refugia is to selectively treat only clinically affected animals, i.e. a system of targeted selective treatment. This may seem to defeat the purpose of anthelmintic treatment for worm control. However, worm burdens are markedly overdispersed within a given flock or herd (Barger 1985), to the extent that in most outbreaks of helminthosis only a minority of animals are unable to withstand the effect of worm infection without anthelmintic treatment. Previously, this phenomenon could not be utilised in practice, since individuals with high *Haemonchus* burdens could only be identified for treatment with the aid of laboratory faecal worm egg count testing which is not feasible, since every animal needs to be tested at relatively short intervals at the height of the worm season. For instance, with severe *H. contortus* challenge of sheep, Malan *et al*. (2001) recorded a drop of up to seven percentage points in haematocrit within seven days. In other words, a sheep which was apparently still coping well with mild anaemia could develop terminal anaemia within less than a fortnight.

It was only after a South African team had devised a system of clinical grading and classification of the anaemia caused by haemonchosis that targeted selective treatment became practical. From the initial results of Malan & Van Wyk (1992) the FAMACHA© system of targeted selective treatment was developed (Bath *et al*. 1996, 2001; Van Wyk & Bath 2002). Highly significant levels of correlation have been demonstrated between the results of clinical FAMACHA© classification and microhaematocrit determination, the laboratory gold standard used to determine an animal's true anaemia status (Van Wyk & Bath 2002). By treating only individuals that are not coping with worm challenge at any given time, the unselected portion of the worm population is given a genetic advantage since, given that highly effective anthelmintics are used, the small numbers of offspring from the survivors of the chemicals in the treated animals are genetically overwhelmed by susceptible worms.

The FAMACHA$^{©}$ method is of course applicable only to haematophagous worm species such as *H. contortus* and, although not specifically tested, probably also to the various hookworms and *Fasciola* spp.

2.3 Optimal application of targeted selective treatment is complex

As pointed out by Van Wyk, Hoste, Kaplan & Besier (2006), the modern methods with potential for countering anthelmintic resistance are unfortunately such that targeted selective treatment and sustainable integrated parasite management are considerably more complex to apply and require greater labour inputs than conventional drenching programmes which could be followed by the farmer, but which also led to the present situation with regards to anthelmintic resistance.

2.3.1 Worm infection not "all-or-nothing"; worm burdens are important

With conventional exclusive reliance on drenching programmes, only a relatively small number of well-spaced treatments was required for good worm control. In contrast, with any system of sustainable integrated parasite management, it needs to be taken into consideration that practically all grazing ruminants are infected with worms practically all of the time (Gordon 1981). The implication for helminths is that, in order to manage worms on a sustainable basis, farmers and their advisors now need to accurately evaluate the relative risk of selection for resistance with use of various formulations of a given anthelmintic, in relation to a variety of factors, such as a move to "clean" pasture, as discussed above and listed in Table 2.2.

2.3.2 Extension services progressively depleted

The complexity of integrated parasite management systems developed over the past decade is compounded by the global decline in numbers of parasitologists and extension personnel with the necessary field experience required for effective technology transfer to farmers, both in developed and developing countries (Van Wyk 2003; Van Wyk *et al.* 2006).

2.4 Can software-based decision-support offer a solution?

Van Wyk and others (Van Wyk 2003, 2006; Van Wyk *et al.* 2006) propose that the solution to the above problems lies in computer based decision-support systems. What is required for regions where there are no well-versed experts, is an automated decision-support system that is so specific that it will lead the farmer in decisions such as whether or not to treat on day X on farm Y when animals are handled, how many of each class of animal to treat; which compounds to use/not to use, the interval before the animals concerned need to be examined again, and how to optimally to integrate all factors with relevance to the farm and conditions at the time.

Without expert knowledge about matters such as the susceptibility of worm populations to available anthelmintics, the relative susceptibility of the class of animal involved to worm challenge, the level of worm infection in the animals, the likelihood of escalating worm challenge during the rest of the worm season, and the relationships between active ingredients and the formulation characteristics of various products, it is virtually impossible to obtain *sustainable* worm management at farm level.

There is no feasible way that farmers can be trained collectively to the level where they will be able, without expert advice, to independently integrate all relevant factors into optimum sustainable worm management decisions at a given time. However, the expert can conceivably be partially replaced by an automated decision-support system.

Various worm management models have been proposed in the past, such as those by Gettinby (1989), Echevarria, Gettinby & Hazelwood (1993), Smith & Grenfell (1994) and Learmount, Taylor, Smith & Morgan (2006), amongst others, which have widely different objectives, and very few models are based on selective treatment of animals. Many parasite models, effective as they are in the hands of experienced statisticians, involve intractable mathematics and/or probability theory. Smith & Grenfell (1994) differentiated between generic models that were simple formulations applicable to whole classes of parasites, and specific models which were more complex and addressed questions regarding particular species. Furthermore, many of these models are also rich in the biological detail of the parasites, addressing issues such as larval survival rate, initial pasture larval contamination, parasite fecundity, and others, all of which require extensive, on-going laboratory sample analysis. The primary objective of many of these models is to predict the timing of the peak worm challenge for a given season, in order to recommend prophylactic or strategic drenching of all animals at a given time, to prevent overwhelming worm infection. Given effective compounds, this is usually highly effective and thus popular with farmers, but it selects severely for worm resistance, especially if the animals are moved to “safe” or “clean” pastures after treatment (Martin 1989; Van Wyk 2001).

Since there were no economically feasible on-farm methods for evaluating the state of worm challenge on which to base decisions on management, it is understandable that only models such as the above were practicable. However, the fact that methods for clinical evaluation of helminthoses, such as the FAMACHA© system, have become available for on-farm use by the farmer, merits re-evaluation of such models. It is suggested that both of what appear to be the main limiting factors for optimal application of targeted selective treatment in sustainable integrated parasite management, namely high labour requirements and complexity, can be addressed through decision-support modelling. In this work, a site specific Monte Carlo simulation model is presented, based on the selective treatment of animals deemed to be anaemic due to haemonchosis. The model differs for the most part from previous models in that it is a published regression model that generates risk predictions for haemonchosis by simulating probable worm burdens in groups of sampled sheep.

2.5 Factors to consider in a computer-based decision-support system

As pointed out by Van Wyk (2006) it is essential for farmers to appreciate that optimum, not maximum, production is the prerequisite for sustainable integrated parasite management. In general, if any animal production system is so far removed from nature that it is not possible to maintain profitable animal production without heavy and total dependence on chemicals, then a change to a more sustainable farming system should seriously be considered (Malan, Horak, De Vos & Van Wyk 1997).

Table 2.2 contains a summary list of factors which would need to be taken into consideration in decisions on worm management, and in Fig. 2.1 interactions for the same are illustrated. From this it is clear that a great many factors interact with one another, and for optimal sustainable integrated parasite management, they should be incorporated into the decision-support process.

Although simulation models are of necessity an over-simplication of the host-parasite system, there has to be a trade-off in terms of how much detail is added to a model in relation to its practical application. For example, can it realistically be used by personnel at farm level for decisions by farmers as to treatment options for given situations of risk of disease? In what format will it be available for use on the farm? How are the results interpreted? The simulation model presented in this work is based on data of the anaemia level and mean body mass of groups of sampled sheep, incorporated into a linear regression model, and simulated by random sampling from the pre-determined statistical distributions of flock haemoglobin level and body mass. The model is simple to apply, and importantly, the results of model simulation have a straightforward interpretation. The model is based on a published linear regression model (Roberts & Swan 1982), which estimates the worm count of sheep by incorporating haemoglobin value and body mass. The preliminary indications are that the simulation model makes biological sense, in that much of what is seen in the field of the progression of haemonchosis over a given worm season by application of the FAMACHA© method can be explained by the two principal inputs of the model, namely haemoglobin value and body mass. It is envisaged that the type of model described here, or a modification of it, would be an integral component in an integrated decision-support system.

TABLE 2.2 Information required for modelling with decision-support software, for *Haemonchus contortus* infection.

(1) FARM LOCATION	Province, District, Grid Reference		
(2) DATE OF EVALUATION	Year, Month, Day		
(3) RAINFALL	(a) Long-term		
	(b) Present		
(4) TEMPERATURE (MIN/MAX)	(a) Long-term		
	(b) Present		
(8) ANIMAL HUSBANDRY	(a) Animal production	(i) Stud	*((i)) BLUP*
			((ii)) Not BLUP
		(ii) Commercial	
		(iii) Resource-limited	
	(b) Animal production type	(i) Breed own lambs	
		(ii) Lambs bought in	
	(c) Principal product	(i) Wool	
		(ii) Meat	
		(iii) Mixed	
(9) PASTURES	(a) Natural	Slope	*((i)) Valley*
			((ii)) Hills/Mountains
		Acocks classification (Acocks 1988)	
		Grazing history	*((i)) Present*
			((ii)) Next paddock
	(b) Improved	Crop species	*((i)) Irrigated*
			((ii)) Not irrigated
(7) ANIMAL HOSTS	(a) Breed		
	(b) Sex		
	(c) Class & Age		
	(d) Identified or not	(i) Identified	*((i)) Indiv. Records*
		(ii) Not identified	*((ii)) Not indiv. Records*
	(e) History	(i) Worm challenge	
		(i) Vaccination	*((i)) Vaccine types*
			((ii)) Dates
	(f) "Drench-all-and-move"?	(i) Yes - After what interim	
		(ii) No	
(5) WORMS	(a) Dominant spp.	(i) Annual cycling	
	(b) Resistance history	(i) Yes - Which anthelmintics affected	
		(ii) No	
(6) DIAGNOSTICS	(a) FAMACHA©	(i) Individual records	
		(ii) Histograms of flock results	
	(b) Haematocrits		
	(c) Worm egg counts	(i) Individual	
		(ii) Composite	
	(d) Host weights & growth		
(10) ANTHELMINTICS ON MARKET	(a) Types	(i) Trade names	
		(ii) Formulations	*((i)) Oral*
			((ii)) Injectable
			((iii)) Bolus
		(iii) Residual efficacy	
(11) MODELLING and TESTING	(a) Data required	(i) FAMACHA©	
		(ii) Haematocrit	
		(iii) Condition Scoring	
		(iv) Worm egg counts	
		(v) Host weights and growth	
		(vi) Climate per farm	
		(vii) Best Linear Unbiased Prediction (BLUP) analysis	

2.5.1 Farm location

In countries such as South Africa, and also in Australia with widely differing climatic zones from a Mediterranean-type climate to subtropics, and where numerous, widely disseminated field trials have been conducted, farm location gives a good indication of the principal worm species to be expected on a given farm (Horak 1981a). It can also be an aid for judging the likelihood of the presence of anthelmintic resistance on the farm. For instance, in communal farming regions in South Africa, where resource-poor farmers predominate, there is generally less anthelmintic resistance than on commercial farms (Van Wyk *et al*. 1999; Vatta & Lindberg 2006).

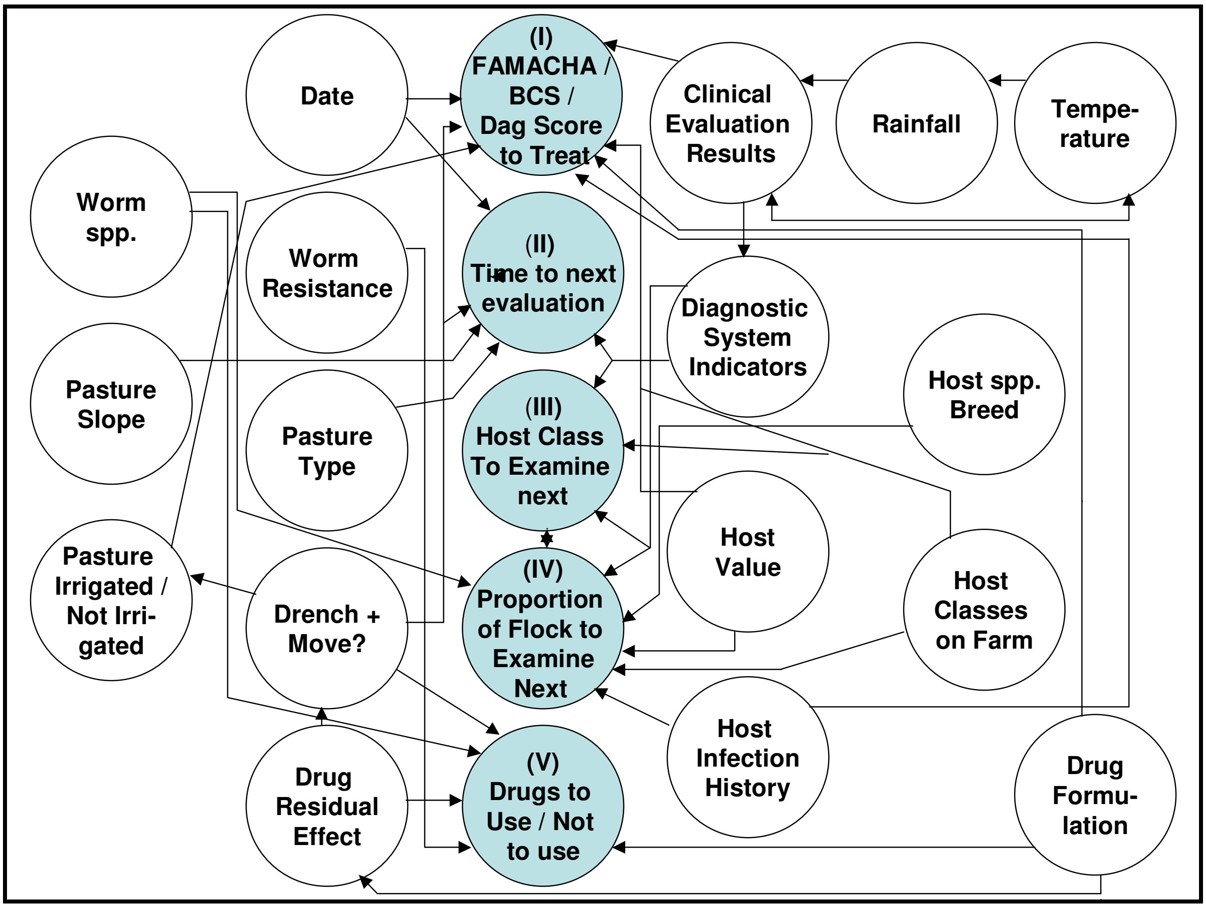

FIG. 2.1 Schematic presentation of factors to consider in arriving at decisions, their interactions with one another, and the envisaged outputs, represented by the shaded circles (I) to (V) for *Haemonchus contortus* infection in sheep.

2.5.2 Rainfall and other sources of moisture

Moisture is one of the main ecological requirements for worms to be able to develop in faecal pellets or pats and translate to pasture. In an attempt to streamline an epidemiological approach to worm management and decisions on anthelmintic treatment, so-called bioclimatographs were produced by earlier workers to delineate combinations of rainfall and temperature conducive to development of different worm species (Gordon 1981). These can at best only be a rough guide to the levels of worm challenge to be expected, since they cannot be used for identifying individual animals which are not coping with worm challenge. Without this, knowledge of conditions which favour worm development can have only limited applicability.

Conventionally, most papers on helminth epidemiology list only total monthly rainfall, and do not give an indication of the daily amount and character thereof in relation to subsequent worm proliferation. However, there is likely to be a threshold of amount of rainfall over time that will be required before the faecal pats or pellets in which infective larvae are contained, will soften sufficiently for the larvae to escape onto pasture and thus be available to their hosts. Consider, for instance, a total of 25 mm of rainfall in a given month. If this amount were to fall as a single shower over a period of one to a few hours it may conceivably be sufficient to soften somewhat moist faecal pats or pellets, but not those exposed to dry conditions for some weeks. Alternatively, if the same amount of rain were to fall over a matter of minutes, run-off may be so fast that the faeces are not softened sufficiently for translation, and on a slope much of the faecal load may conceivably be washed away into streams or distant pools and the worm larvae thus be lost to the hosts from which they originated. On the other hand, if the rain were to fall in four equal showers which are spaced evenly over the course of a month at 6 mm per week for four weeks, it seems unlikely that the faeces would become sufficiently softened to set entrapped larvae free.

It is proposed that the amount and character of rainfall be studied in relation to levels of worm infection, to get an indication of the threshold amount/distribution of precipitation required for larvae to be able to escape from faecal deposits. Rainfall can, for instance, be classified according to periodic amounts, as well as dispersion and character in relation to observed helminth epidemiology. This is discussed in Chapter 6 where the Shannon entropy model is applied to rainfall data, in order to determine an index of the spread and evenness of rainfall during inter-sample periods. It also seems likely that satellite imagery will be of help as an indication of rainfall amount and effect, and thus of the extent of worm development to be expected from time to time, as well as the proportions of animals that should be treated in any targeted selective treatment worm management system.

2.5.3 Temperature

Temperature is one of the principal determinants of the seasonal cycling of different species of helminths (Veglia 1915; Gordon 1981). At lower temperatures larval development within eggs either ceases or is considerably delayed, or the eggs may die (Rose 1970). However, rising temperature during spring and summer progressively speeds up development until worm eggs hatch in an intensive wave, the so-called concertina effect (Rose 1970). In general, once the worm eggs have hatched and the emerging larvae have developed to L_3, the latter are less susceptible to extremes of temperature than are the undeveloped eggs.

2.5.4 Animal hosts

Host species and breed

There are important differences between both the species and the breed of the host in relation to worm infection (Baker, Mwamachi, Audho, Aduda & Thorpe 1999). If two host species such as sheep and horses are alternated on pasture or run together on the same pasture, they tend to control each other's helminths by ingesting larvae, which cannot propagate themselves in the "wrong" host and thus die.

Host reproductive status

In the initial trials designed to test the principle of clinical evaluation of the anaemia of haemonchosis according to the colour of the ocular mucous membranes it was shown that while 83 % of dry, non-pregnant ewes were able to withstand severe worm challenge unaided, only 70 % of heavily pregnant and 45 % of lactating ewes in the same flock were able to do so (Malan *et al*. 2001). This phenomenon has important implications not only for decision-support modelling, but also for labour saving in targeted selective treatment application.

In early targeted selective treatment trials and field investigations, all classes of sheep were treated similarly as regards intervals between clinical evaluations and FAMACHA© classes to treat (Malan *et al*. 2001; Van Wyk *et al*. 2001; Van Wyk & Bath 2002). Instead, the sharp differences in susceptibility of the different classes hold the potential that intervals between clinical evaluations be set according to the most susceptible classes in flocks. Labour can then be considerably reduced by examining only these animals until such time as there are indications of mounting worm challenge, at which time other classes can be included. Such an approach can progressively contribute considerably to labour-saving in field use of targeted selective treatment, which is a serious limitation at present.

Host age

The conjunctiva of the lower eyelid, which is the correct spot to view for FAMACHA© evaluation, is considerably more difficult to inspect in suckling lambs than in adult sheep and goats (J.A. van Wyk, personal communication 2005). Farmers are reluctant to handle such young lambs at the relatively short intervals required at the peak of the *Haemonchus* season. Thus, allowance needs to be made for this in recommendations and also in any intended model. A possible solution is to treat all suckling lambs when severe worm challenge is likely, or else to examine only a few of the lambs and to treat all if the proportion of FAMACHA© category 1 animals is lower than, say, 80 % or 90 %. Such treatment of lambs should have little effect on selection for anthelmintic resistance, on condition that their mothers are not treated at the same time and can therefore maintain worms in refugia. To some extent there is support for this type of approach from New Zealand. Despite five drench treatments at 28-day intervals where all but 10 % of lambs (the heaviest lambs were left undrenched) were drenched in a trial, Leathwick, Waghorn, Miller, Atkinson, Haack & Oliver (2006) found no significant differences in live weight gains between drenched and undrenched lambs after the last two treatments. However, they also reported that either leaving a proportion of the lambs undrenched or drenching lambs only when faecal worm egg counts exceeded a threshold level failed to create a measurable pool of unselected larvae for some parasite species.

History of a given flock

Irrespective of the results of FAMACHA© evaluation at a critical time, such as immediately pre-winter in relatively wet summer rainfall regions where the nutritional value of pasture becomes severely reduced in winter, decisions on which clinical categories of animals to treat must take the relative level of worm challenge experienced by the flock in the current worm season into consideration in the case of targeted selective treatment. The level of worm infection in late autumn and winter in summer rainfall areas will generally be considerably higher than with most systems of conventional programmed drenching, and worm burdens which are well tolerated in summer could then seriously affect animals when the pasture deteriorates nutritionally. The history of infection is also of importance in decisions concerning clinical categories of FAMACHA© to treat, for instance when animals are moved to "clean" grazing before being treated.

Stud or commercial flock

In general, stud sheep and goats are worth more than commercial animals, and this has to be allowed for when formulating recommendations on questions of risk. When balancing risk with labour saving in relation to intervals between clinical evaluations of a given flock, this needs to be considered. Stud breeders and the management of experimental farms are also more inclined to drench their animals excessively, with the result that the worm populations on such farms are more likely to be resistant than on most other farms (Van Wyk, Van Schalkwyk, Bath, Gerber & Alves 1991). For such farming systems it will therefore be more important in the required decision-support software to emphasise worm resistance testing than otherwise. Stud animals are also invariably individually identified, with the result that it is easier to track and subsequently cull overly susceptible individuals than in commercial flocks, where animals are often not individually identified. On the other hand, with planned global introduction of "farm-to-fork" identification of farm animal products this difference is likely to disappear in the near to medium future.

2.5.5 Pastures

Pastures play a crucial role in the epidemiology of gastrointestinal helminth infections, and a variety of factors will have to be taken into account in models aimed at an automated decision-support system.

Number of paddocks

The more paddocks there are available on a farm, the more scope there is for planning movements of animals to minimise the levels of worm challenge in a given worm season, provided that record keeping of animals frequenting each paddock over time is implemented. For instance, given a multitude of paddocks and availability of both sheep and cattle, in the case of the so-called "50-50" grazing system (Kirkman & Moore 1995) where half the available grazing lies fallow for up to a year, sheep can be moved repeatedly "ahead" of accumulating worm numbers. The paddocks vacated by sheep can then be used to graze cattle or horses, to allow longer periods of time before the sheep return to the pastures they infected previously (Moore & Van Wyk 1997). In this way most classes of sheep will be able to manage with almost no drenching, especially if targeted selective treatment is practised, without compromising profitability as regards optimum utilisation of pastures (Michel 1976, 1985).

Pasture type - current paddock and planned movement to the next paddock

Improved pastures have a greater carrying capacity than natural pastures, particularly if irrigated, providing optimised conditions for a substantial build-up of worms and serious challenge to susceptible hosts. Michel (1976, 1985) does point out, however, that higher concentrations of hosts on pasture do not necessarily lead to higher worm challenge, given optimum utilisation of pasture. In the latter case animals are withdrawn when the available herbage has been utilised to the level where animal production levels off, and the animals return only once sufficient re-growth has occurred for optimum animal production. Thus, numbers of animals on a given pasture can be expected to be reciprocal with grazing period and pasture contamination with worms can optimally be expected to be unaffected by grazing pressure.

Pasture herbage species

Within reason, the more edible bushes, shrubs and trees there are on pasture and the more animals browse, the lower the build-up of worm infection that is to be expected. In South Africa, for instance, Horak, Knight & Williams (1991) and Horak, MacIvor & Greeff (2001) reported negligible numbers of worms recovered from Angora goats with ample browsing on "Valley Bushveld" pasture in the Eastern Cape Province, a region where the climate is otherwise conducive to heavy worm infection in both small ruminants and cattle that do not have access to edible bushes and trees for browsing (Horak 2003; Horak *et al*. 1991, 2001; Horak, Evans & Purnell 2004). Additionally, some tannin-rich plants such as *Lespedeza cuneata* have antiparasitic properties, but the most commonly observed effect of bioactive forages is depressed worm egg counts (Hoste, Jackson, Athanasiadou, Thamsborg & Hoskin 2006). Other effects, such as reduced nematode numbers and parasite fecundity, may be of value in sustainable integrated parasite management if these can be shown to be consistently obtainable when bioactive forages are made available to sheep.

Pasture grazing history

Season, type and amount of rainfall, periods of grazing and class of animals involved all have an important bearing on the role pasture will play in the levels of worm infection experienced by grazers and hence the potential to result in overwhelming levels of worm infection in grazing animals. For instance, pastures grazed by weaner lambs in autumn in a Mediterranean-type climate will constitute a considerable risk for susceptible classes of sheep in the ensuing spring and early summer (Michel 1976). On the other hand, the opposite is true in the so-called 50-50 grazing system of Kirkman & Moore (1995) and Moore & Van Wyk (1997) in South Africa, where all the animals on a given farm are concentrated on half of the available pasture for up to a full year, with the other half lying unutilised in the interim, and is therefore almost worm-free when animals are returned to it after the rest period. If animals are drenched directly before they are moved to this pasture, severe selection for drug resistance is likely to occur since the pasture will be populated primarily by the offspring of worms which withstood the drench. Note, however, that in the tropics, in contrast, removal of animals from pasture for as short a time as a month will also lead to practically “clean” pasture (Barger 1994).

2.5.6 Worm species and anthelmintic resistance

Dominant worm species and their susceptibility to anthelmintics will dictate the measures required for avoiding losses, and an intimate knowledge of these factors will be a pre-requisite for any system of worm management. Provision will have to be made for winter rainfall regions such as the eastern and southern Cape in South Africa (Horak 2003; Horak *et al*. 1991, 2001, 2004). In relatively arid regions with erratic and highly variable amounts of summer rainfall per year, such as the Kalahari semi-desert in southern Africa, outbreaks of haemonchosis are uncommon (J.A. van Wyk, personal communication 2005), but tend to occur unexpectedly from time to time when good rain falls.

2.5.7 Diagnostic methods

As noted above, targeted selective treatment requires that animals be examined repeatedly during the worm season. In the case of *Haemonchus* sp., evaluation of relatively large numbers of animals needs to be done at short intervals during the peak worm season to prevent losses of excessively susceptible individuals. This automatically excludes any known laboratory test on the ground of impracticality and leaves only methods of clinical evaluation such as FAMACHA©. No single method of clinical evaluation is sufficient on its own for use with mixed worm infections, since methods of clinical evaluation are needed for both bloodsucking and non-bloodsucking worms such as *Teladorsagia* and *Trichostrongylus*. For this reason provision must be made in the system for a variety of methods, such as FAMACHA© and weight-change based evaluation.

2.5.8 Anthelmintics to use or avoid

Correct use of anthelmintics for obtaining an optimal balance between worm management and minimal selection for drug resistance is dependent on a variety of factors. It is difficult to convince farmers to buy anthelmintics according to active ingredient rather than on trade name. In South Africa even the listing of the activity group by number on the label of every registered anthelmintic has apparently not overcome this problem. Furthermore, each farmer breeds his or her own "brand" of resistance according to the drugs used over time and the circumstances in which they are used. Formulations for a given compound may differ considerably, for example benzimidazole drenches compared to slow-release boluses.

While short-acting formulations like some benzimidazoles may be ideal for a specific set of circumstances, sustained release formulations of these compounds may be contra-indicated. For instance, it is unlikely that the ultra long-acting moxidectin which was introduced to the market recently, with the claim of being "highly effective" for a period of three months against *H. contortus* in Australia and four months in South Africa, can be used without selecting severely for resistant worms. Although the best short-term option from the point of view of the farmer may be to use a persistent anthelmintic that achieves a substantial reduction in worm burden, this strategy is not sustainable because a high proportion of the worms accumulating in the sheep are resistant (Le Jambre, Dobson, Lenane & Barnes 1999). Hence it will be necessary for the envisaged decision-support model for each different situation to list by both trade name and active ingredient all the registered drugs which are recommended, excluding others regarded as unsuited to the occasion.

2.5.9 Treatment in relation to movement of animals to other pastures

Conventionally, animals are drenched strategically at the time of a move to rested pasture (Theiler 1912; Michel 1976). If the move occurs soon after anthelmintic treatment and the animals do not become re-infected with unselected worms in refugia before the move, severe selection for anthelmintic resistance takes place if the pasture to which they are moved is uninfected. Even though this is well known, it is difficult to formulate recommendations for avoiding this possibility. Because of the large differences in residual action between different formulations of a given compound it is not possible to recommend, for different compounds or formulations the general time periods that must be allowed between drenching and the intended move. For this reason Molento, Van Wyk & Coles (2004b) propose that in the case of a move to safe or "clean" pasture the animals are not dewormed before, but only after the move, with the time before treatment on the new pasture to be dictated by the level of infection of the animals at the time they are moved.

2.6 Modelling approach

The envisaged decision-support software model will need to address a variety of questions for optimal worm management (Table 2.2), with a complex system of interactions between them (Fig. 2.1). An important consideration is that presently available methods for application of targeted selective treatment are relatively labour intensive in addition to being complex. In the light of the large variety of interacting factors that need to be considered in an automated decision-support system provision must be made in the model for use of both specific data and also expert opinion until sufficient data has been generated.

2.6.1 Retrospective analysis of clinical evaluation data

The nature of methods used for identifying stragglers in a given flock for drenching leads to a multiplicity of data sets by the time worm challenge becomes serious in any worm season. For instance, in the case of the FAMACHA© system, expressing the proportions of the various categories in the form of a histogram graph makes it possible to follow the progressive adverse effect of mounting worm challenge (Fig. 2.2). With retrospective analysis of the results, drenching can be adjusted to include more or fewer FAMACHA© categories to ensure that the animals are not overwhelmed. At the same time allowance can be made for the optimum number of undrenched animals to produce sufficient numbers of free-living helminth stages in refugia for sustainable management. This is addressed in

Chapter 3 with sensitivity analysis, and in Chapter 4, where Receiver Operating Characteristic analysis was applied to FAMACHA© trial data. As an example, while the general recommendation has thus far been to routinely treat all sheep and goats evaluated to be in FAMACHA© categories 3–5, this can be adjusted at the height of the worm season to include animals in FAMACHA© category 2, or, if this adjustment does not succeed in reversing the tendency to increasing severity of helminthosis, all animals can be treated.

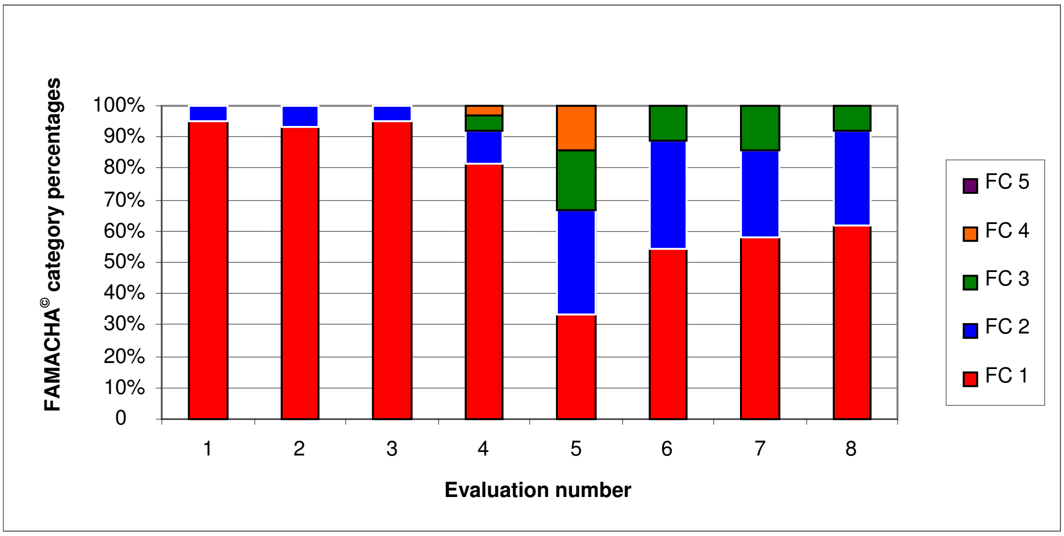

FIG. 2.2. Example of FAMACHA© results for eight evaluations over a *Haemonchus* season in South Africa for a group of 130 ewes; FAMACHA© category 5 not present (FC = FAMACHA©).

2.6.2 Model framework

Labour saving would be one of the aims of the intended model. As discussed above, it would require, from retrospective analysis of clinical evaluation data, to recommend the minimum levels of drenching which will prevent excessive losses in the production of the animals concerned, while allowing the optimum numbers of worms in refugia. Labour saving can be achieved, amongst others, by estimating the maximum safe interval between clinical evaluations according to season and risk factors, such as rainfall and temperature, during the period immediately preceding the point of the decision, and the minimum proportions of animals to be examined per flock (Table 2.2).

2.7 Effective technology transfer

2.7.1 Technology transfer previously ineffective

Unabated escalation of anthelmintic resistance, despite the availability of effective countermeasures (Van Wyk *et al*. 2001; Rhodes *et al*. 2006) indicates that efforts at technology transfer to both farmers and scientists are possibly inadequate. Despite an emphasis on various methods of integrated parasite management instead of dependence only on drenching for worm control, the majority of farmers still depend almost exclusively on chemical control, with the excuse that losses in production could result with adoption of available alternatives. While it was clearly shown in the 1980s that strategic drenching at a stage when there are few free-living worm stages in refugia selects severely for anthelmintic resistance (Martin *et al*. 1981; Martin 1989), this was largely ignored until the beginning of the present century (Van Wyk 2001). Even today, a variety of advertisements concerning worm management ignore the concepts of refugia and sustainable integrated parasite management, and propagate drug sales at the cost of sustainability of worm management (Van Wyk 2003).

The most important reasons for the failure of technology transfer are a combination of complexity of alternatives to the simple drenching programme and a shortage of the necessary extension personnel. There have also been many different anthelmintics available to the consumer, leading to the problem that both farmers and their advisors have refused to give credulity to early warnings on anthelmintic resistance. While the possibility of resistance of worm populations to all available compounds was predicted more than twenty years ago (Van Wyk 1985), this was regarded by many as alarmistic (Van Wyk 1990). It is apparently only when there are signs of total failure of anthelmintics on their own farms that most farmers are prepared to consider simple drenching programmes (Van Wyk, Malan & Randles 1997b). The fault does not lie entirely with the farmer, however. Worm management is more complex than for most diseases against which there are effective vaccines and farmers need to be given large amounts of basic information on worm management to be able to “translate” on-farm observations and results into optimum sustainable worm management.

2.7.2 New approach required

The use of software-based decision-support which is specific to time and place and contains recommendations on issues such as drugs to use, categories of animals to treat, and intervals between clinical evaluations, could be effective for technology transfer to individual farmers (Van Wyk 2003, 2006). With this approach it should not be necessary to train farmers or their advisors to the level of being able themselves to evaluate the complexities of the optimum period between treatment and movement of animals in accordance with the drug formulation used, as this can in theory be managed by dedicated software.

Sufficient relevant data has been generated in most countries to form the basis for development of the suggested software and the technology for on-farm application is already available even for regions with practically no infrastructure, other than access to electricity. Most commercial farmers use computers for farm and stock management on a daily basis, and satellite transmission can be employed for resource-poor communal farmers where landlines are absent or not dependable. A relatively inexpensive option for the latter farmers is to provide their veterinary and agricultural extension advisors with the necessary equipment and, as suggested above, make provision in the software for decisions based on expert opinion utilising estimates of factors such as rainfall and temperature where specific data is not available. The computer-generated decisions could then be communicated to communal farmers via cell (mobile) phone.

In the light of ubiquitous poverty it may seem unlikely that the per capita use of cellphones in Africa appears to be the highest in the world. However, cellphone use is generally higher in developing, compared to developed, countries (J. Britz, University of Wisconsin-Milwaukee, personal communication 2005). For instance, by 2001 mobile subscriber numbers in Africa had overtaken those of fixed lines, the first region of the world to achieve this. In addition, the effect of GSM ("Group Special Mobile", or wireless) technology is twice as big in developing nations as in their developed neighbours (Anonymous 2005). A special consideration is that farming activities in many, if not most, resource-poor farming communities are centred around easily accessible farmers' committees. In other instances communication between these farmers and their advisors can proceed by whatever means used at present.

The technology required for the satellite access suggested above is inexpensive in relation to the considerable potential of such a decision-support system for specific, accurate technology transfer. Broadband Global Area Network (BGAN) in South Africa recently quoted US$7 per Mb of data downloaded and a monthly charge of US$30. While these tariffs are expensive if large amounts of data are to be downloaded, only relatively small volumes of downloading will conceivably be required for instituting a worm management system via satellite, since once the software is loaded, it is likely that little else will be required until it needs to be updated. In other words, we need to move on from software that provides general information by region, to specifics tailored not only to the individual farmer, but more precisely to day-day decisions on worm management by that farmer.

2.8 Discussion

For both the resource-poor and the commercial farmer there is an urgent need for decision-support software, to a large extent to neutralise the sales pressure of drug manufacturers and their representatives. For the commercial farmer it is a matter of attempting to retain efficiency of at least some of the modern-day anthelmintics. For the resource-poor the prime consideration is to avoid many of the mistakes made in the commercial farming sector. Developing farmers are inclined to buy animals from commercial farmers to improve their stock, in which case excessive drenching can be expected to decrease the frequency of occurrence of susceptible genes and allow only the ones conveying drug resistance to pass.

The principal advantage of using clinical methods of analysis such as FAMACHA© is that without the need for laboratory intervention, a series of results are obtained on-farm by the farmer himself as a given worm season progresses, on which decisions can be based for risk-evaluated sustainable integrated parasite management. Through retrospective analysis of results in a simplistic way, to depict consecutive FAMACHA© results in series of bar graphs, it is possible to visually follow changing ratios between the various FAMACHA© categories as an indication of developing anaemia (Fig. 2.2). This is a fundamental deviation from conventional models for worm control, which have thus far practically all been based on predicting, at the start of a given worm season, the levels of worm infection to be expected, and then applying anthelmintics prophylactically in a way which did not make provision for a build-up of worms in refugia before chemical prophylaxis was instituted. In contrast, when targeted selective treatment is applied as suggested, untreated animals provide growing pools of helminths in refugia. Even if all the animals need to be given a treatment in midworm season, the pools of larvae in refugia are available for re-infection, as long as long-acting formulations of anthelmintics are avoided (Van Wyk 2001).

It is clear from Table 2.2 that the inclusion of the vaccination history of the animals concerned could allow an automated decision-support system to be broadened to include other aspects such as external parasites and infectious diseases in general. As a first step, however, the presently envisaged software is aimed primarily at internal parasites in small ruminants.

2.9 Conclusion

Anthelmintic resistance is so advanced at present that drastic counter-measures are required, especially as regards present methods of technology transfer. Every effort should be made to have alternatives in place, should new anthelmintics perhaps become available in future, in an effort to prevent a recurrence of the failure of the macrocyclic lactones, to which resistance was recorded within a period of three years of the first member of the group having been introduced to the market for sheep (Carmichael, Visser, Schneider & Soll 1987; Van Wyk & Malan 1988).

Thus far anthelmintic resistance has largely been confined to the worms of small ruminants and horses, for which the global market for anthelmintics is too small to counter the high financial risk of development of drugs in unrelated new activity groups (McKellar 1994). However, it is to be expected that what appears to be an increase in anthelmintic resistance in the worms of cattle (Caracostantogolo *et al*. 2005; Rhodes *et al*. 2006) will have the effect of stimulating drug firms to resume development of unrelated new compounds. It is essential to have methods for preventing a repetition of the mistakes of the past as regards anthelmintic usage in place before any such new compounds reach the market.