MODULE 4. MITES: ACARICIDE RESISTANCE: DIAGNOSIS, MANAGEMENT AND PREVENTION

1 INTRODUCTION

Scabies (mange) has remained for centuries a disease of economic importance affecting animal production and welfare. Most types of mange are forms of allergic dermatitis, characterized by encrustation, alopecia, and pruritus, initiated and maintained by a number of mite species. All the major mange mite species are contained within the orders Astigmata and Prostigmata. The Astigmata are a well-defined group of slow-moving, weakly sclerotised mites, including the medical or veterinary important families Sarcoptidae and Psoroptidae. The Prostigmata include the Trombiculidae (harvest mites), parasitic as larvae but free-living predators in the nymphal and adult stages, and the true mange mite families Cheletoidea (*Psorobia* (*Psorergates*) sp.), Demodicidae (*Demodex* sp.) and Cheyletiellidae (*Cheyletiella* sp.). The latter (being parasites of companion animals) are of no direct significance to livestock production. Worldwide losses from mange mites on livestock production have been estimated to amount to US$14.4 million (Drummond *et al*., 1981).

Psorobic mange

Two species of *Psorobia* have been isolated from domestic animals: the benign 'parasite' *P. bos* from cattle and the more important *P. ovis*, occurring in Merino sheep in Australia, South Africa and South America. Most mites are found under the stratum corneum in the superficial layers of the skin of the sides, flanks and thighs, feeding on the exuding fluid. The infested area is dry and scurfy; wool fibres break easily, with the remaining wool coming together as ragged tufts. Irritation causes the sheep to rub and kick the affected area and chew its fleece, resulting in "fleece derangement" and downgrading of the wool clip.

Demodectic mange

Demodex are easily recognized by their annulate, vermiform ("worm-like") shape, but may be overlooked on account of their small size. *Demodex* inhabit the hair follicles and the sebaceous and meibomian glands of the skin of a number of wild and domesticated mammals, including humans. Different species occur on different hosts, and more than one species may occur on the same host. Two species have been isolated from sheep. *D. aries,* is a benign commensal of the follicles and sebaceous glands of the feet, face, eyelids, ears, prepuce and vulva and *D. ovis* lightly parasitises the hair follicles and sebaceous glands of primary hairs over the entire body, with highest populations occurring on the neck, flanks and shoulders. Infested follicles become distended with mites, mite exuvia, eggs and epithelial cells, forming nodules, and pyogenic bacteria convert these nodules into pustules. Skin with advanced lesions is thick and scaly, alopecic, nodular or pustular. Itching may stimulate kicking, biting and rubbing of the lesions. In general the disease is of low incidence and of little importance (Desch, 1986). On cattle, demodicosis occurs as flat nodules in the skin with a massive enlargement of the sebaceous glands, which contain vast numbers of *Demodex* mites. Demodicosis (*D. bovis*) was recorded as the most common skin defect in Kenyan, Tanzanian and Ugandan cattle hides (Bwangmo, 1969).

Sarcoptic mange

Mites in the family Sarcoptidae are obligate parasites, burrowing into the skin of mammals. The itch mite (*Sarcoptes scabiei*) is the cause of scabies in humans and mange in a wide range of domestic and wild mammals throughout the world, generally affecting the sparsely haired parts of the body. The number of species within the genus is still open to debate. Studies of populations of *Sarcoptes* mites from a wide range of hosts have suggested that there is only one type species

(*Sarcoptes scabiei*) with a number of variants infesting a wide range of mammalian hosts (Fain, 1968). Recent investigations based upon molecular analysis of the ITS-2 of the mRNA gene suggest that the genus *Sarcoptes* is monospecific (Zahler *et al*., 1999).

S. scabiei var. *suis* is one of the most important skin diseases in pigs worldwide, with reported losses in the United States estimated at US$200 million per annum (Hogg, 1989). Sarcoptic mange is endemic in pig herds throughout the European Union and a number of member states have active eradication programmes (e.g. Belgium, Denmark and Holland) and according to the Swedish Animal Health Service, pigs sold as fatteners must be certified free from sarcoptic mange. In 1991 sarcoptic mange was identified in 27.9 percent of British breeding herds and 67 percent of finishing units (Anonymous, 1989a), with the majority of cases sub-clinical and restricted to the inside of the pinnae. Sarcoptic mange is likely to be present in most herds unless derived from specific pathogen free (SPF) sources (Dobson and Davis, 1992).

S. scabiei var. *bovis* affects cattle world-wide with infestations generally located at the base of the tail, the inner thigh, under the neck and the brisket. Although disease is generally sub-clinical in the United Kingdom, generalized infestations can occur (Bates, 1997). In sheep, sarcoptic (head) mange, caused by *S. scabiei* var. *ovis* has been recorded in Europe, Africa, the Middle East, the Balkans, India and South and Central America (Bates, 2000a). *S. scabiei* var. *ovis* is found on the sparsely haired parts of the body, such as the face and ears. Mites burrow into the epidermis and feed on tissue fluids. The burrowing and feeding of the mite causes irritation and consequential scratching, leading to inflammation and exudation to form crusts. Small foci of infection do not appear to affect the health of an animal adversely but can be more serious if the condition spreads. *S. scabiei* can temporarily infest humans (Bates, 2000a).

Family Psoroptidae

Mites in the family Psoroptidae are oval, non-burrowing mites, parasitic on mammalian skin. Three genera, *Psoroptes*, *Chorioptes* and *Otodectes* are of veterinary importance, although the latter (being a parasite of the ears of carnivores) is of no direct significance to livestock production.

Chorioptic mange

Mange caused by species of *Chorioptes* is more localized and often asymptomatic and is therefore not as serious as that caused by *Sarcoptes* or *Psoroptes*. Reservoirs are found on the fore and hind pasterns (Baker, 1999) and from these areas mites can spread to the rest of the body.

Two species of *Chorioptes* are recognized: *C. bovis*, infesting cattle, goats, horses, sheep and rabbits and *C. texanus* recorded on goats, reindeer and cattle (Rosen *et al*., 1989; Sweatman, 1957). In cattle, chorioptic mange commonly occurs on the base of the tail, the perineum, and the back of the udder. The hooves may also be affected, resulting in lameness. Heavy infestations can cause loss of condition, which can lead to emaciation and damage to hides (Walker, 1994).

Chorioptes infestations of the major breeds of cattle in the United Kingdom (Hereford, Holstein Friesian, Jersey, etc.) are generally asymptomatic, but the mite can be a cause of extensive mange on continental cattle breeds (Limousine, Charolais, etc.), particularly in bulls. This form of mange is an extreme form of allergic dermatitis and the gross symptoms can easily resemble bovine psoroptic mange. Symptoms include a thick crusty scab and intense irritation. The scab itself may affect the efficacy of synthetic pyrethroid pour-on acaricide formulations, by acting as a sponge and absorbing the formulation at the site of application, thus preventing translocation around the body (Bates, 1997).

A low incidence of foot and scrotal mange due to *C. bovis* has been recorded in Australian and New Zealand sheep. In the late 1960s the parasite was found to have infested the pasterns of

sheep in the United Kingdom (Bates, 2000a) and was thought to have been eradicated following 18 years of compulsory dipping for sheep scab (*P. ovis*), but the parasite has recently been recorded as the cause of scrotal mange on Suffolk rams (Sargison *et al*., 2000).

Psoroptic mange

Although *Sarcoptes* and *Chorioptes*, and to a lesser extent *Demodex* and *Psorobia*, can be regarded as having significant effects on animal production (particularly *Sarcoptes* on pig production), *Psoroptes ovis* is by far the most damaging and cosmopolitan mange mite.

P. ovis are non burrowing, cosmopolitan, obligate ectoparasites, causing a debilitating dermatitis, involving hair or wool loss and a pruritic scab formation. The parasite occurs in all the sheep and cattle rearing countries of the world, although it was eradicated from Australia and New Zealand towards the end of the nineteenth century (**Table 1**). Infestations on sheep (sheep scab) can be a cause of considerable suffering and even mortality within infested flocks. Flock productivity can be severely affected, either directly through reduced lamb crops or downgraded wool or leather, or indirectly through the use of expensive chemical control programmes with their associated withholding periods for meat, milk or fleece. In Argentina, psoroptic mange is the most damaging ectoparasitic disease affecting domestic livestock. In 1989 the estimated annual losses ranged between US$100 million in cattle and US$150 million in sheep (Nuñez, 1989).

Table 1. Status of sheep scab throughout the world

Country	Date eradicated	Date returned
Argentina	Never eradicated	
Australia	1896	
Austria	Never eradicated	
Brazil	Never eradicated	
Canada	1927	
Denmark	1929	1979
France	Never eradicated	
Germany	1948	1973
Hungary	1965	1978
India	Never eradicated	
Iran	Never eradicated	
Lesotho	1935	1973
New Zealand	1885	
Norway	1894	
Republic of Ireland	Never eradicated	
Saudi Arabia	Never eradicated	
South Africa	Never eradicated	
Swaziland	Never eradicated	
Sweden	1934	
Uruguay	Never eradicated	
United Kingdom	1953	1973
United States of America	1973	

Five species of *Psoroptes* are recognized (Sweatman, 1958): *P. ovis*, a body mite causing mange in sheep, cattle and horses, *P. equi*, a body mite of equids, *P. natalensis* a body mite of cattle and horses, *P. cuniculi* the ear mite of rabbits, goats, horses and sheep and *P. cervinus* an ear mite of bighorn sheep, elk and wapiti. A sixth, invalidated, species is *P. auchinae*, an ear mite of new world camelids. Like the genus *Sarcoptes*, the numbers of species in the genus *Psoroptes* is open to debate, *P. ovis* and *P. cuniculi* may be variants of the same species (Bates, 1999a).

Psoroptes on rabbits

Ear canker, caused by *P. cuniculi*, is a common disease of domestic rabbits throughout the world. In Egypt mange (sarcoptic or psoroptic) in rabbits is considered to be second to coccidiosis in importance, with high losses reported (Ezzat, 1955). In Great Britain the parasite is extremely common in pet rabbits and commercial rabbit colonies, either for meat or laboratory rabbit production. Infestations appear to be confined to domestic rabbits. Surveys of ectoparasites of wild rabbits in Great Britain (Bates, 1999b) and Australia (Mykytowycz, 1957; Williams, 1972) have not recorded *P. cuniculi*, but it is not clear whether the Australian surveys included an examination of the ears (Strong and Halliday, 1992). The only report of psoroptic otoacariasis occurring in wild rabbits was in France (Guilhon, 1990). Lesions are usually confined to the ear canal or internal aspects of the pinnae but infestations can spread out of the ear canal to produce extensive, clinical lesions of the entire pinnae, the base of the ears, the cheeks, dewlap and face. Lesions and mites can also be present between the digits of both hind feet (Bates, 1999b). Secondary infections have been recorded, including otitis media and otitis internal, torticollis, ulcerous meningocephalitis accompanied by abscessation of the medulla oblongata region and interference with the central nervous system (Von Ribbeck and Ilchmann, 1969). Changes in the tympanum of infested rabbits attributed to *P. cuniculi* and mites have actually been seen in the immediate vicinity of the brain of an infested rabbit (Von Ribbeck and Ilchmann, 1969).

Psoroptes on goats

P. cuniculi (synonym *P. caprae*) has been reported in Australia (Roberts, 1952), Bangladesh (Nooruddin and Mondal, 1996), Brazil (Faccini *et al*., 1981), Canada (Lofstedt *et al*., 1994), Fiji (Munro and Munro, 1980), India (Shastri and Deshpand, 1983), Israel (Yeruham *et al*., 1985), Italy (Perrucci *et al*., 1996), New Zealand (Heath *et al*., 1983), South Africa (Shilston, 1915), Sudan (Abu Samra *et al*., 1981), British Isles (Littlejohn, 1968; Bates, 2001), United States (Williams and Williams, 1978) and Zimbabwe (Odiawo and Ogaa, 1987). Most infestations are subclinical, asymptomatic (other than the occasional episode of ear scratching with the hind feet) and are easily overlooked (Bates, 2001; Schillhorn van Veen and Williams, 1980). *P. cuniculi* has been isolated from the external ear canals of feral goats in Australia and New Zealand (Heath, 1979; McKenzie *et al*., 1979; Hein and Cargill, 1981). Ovine psoroptic mange (sheep scab) is not endemic to either Australia or New Zealand and *P. cuniculi* in the ears of goats are not therefore considered a reservoir of infestation.

In meat and dairy goats infestations are usually confined to the ears. Transmission can occur between mother and offspring as early as five days after birth (Heath *et al*., 1989) and is a function of age, with the highest infestation in animals between 6 and 12 months old (Bates, 2001). Infestations are generally confined to the external auditory canal, which can be plugged with thick, brown, laminated scab, close to the tympanic membrane (sometimes completely occluding the canal) although no damage to the tympanic membrane has been observed at post mortem (Williams and Williams, 1978; Odiawo and Ogaa, 1987). The waxy plug deep within the external auditory canal contains *Psoroptes* mites of all stages. Infestations (often classified as *P. caprae*) have also been recorded to involve the entire pinna, or spread to form body lesions, involving the poll, neck, withers, back, abdomen, pasterns and inter-digital spaces (Lofstedt *et al*., 1994; Munro and Munro, 1980; Littlejohn, 1968). *P. cuniculi* has also been shown to be capable

of carrying mycoplasmas (possibly pathogenic) between goats (Cottew and Yeats, 1982; Da Massa, 1990).

In Brazil the prevalence of infestation and number of mites per host were higher in goats than in sheep (Faccini and Costa, 1992). There is a possibility that *P. cuniculi* may not be host specific and may freely transfer between the ears of sheep and goats, given the correct set of circumstances (Williams and Williams, 1978; Sweatman, 1958). There is little evidence for the goat strain of *P. cuniculi* causing clinical sheep scab. Artificial and natural exposure of sheep to *P. cuniculi* infested goats has never resulted in classical sheep scab (Williams and Williams; Heath *et al*., 1989; Sweatman, 1958). This is supported by the fact that *P. cuniculi* is common in domestic and feral goats in Australia, New Zealand and the United States (Roberts, 1952; Heath *et al*., 1983; Williams and Williams, 1978; Schillhorn van Veen and Williams, 1980; Heath, 1979; McKenzie *et al*., 1979; Hein and Cargill, 1981; Heath *et al*., 1989; Cottew and Yeats, 1982; Cook, 1981; Friel and Greiner, 1988) where sheep scab has been eradicated and ovine psoroptic otoacariasis has not been recorded. Evidence for the transfer of scab mites to goats is not so well documented. The hair coat of dairy goat breeds may not be suitable for maintaining the optimal microclimate for mite survival and thus colonization by *Psoroptes* mites. The long fibres of Angora goats may be more conducive to mite survival. *P. cuniculi* is capable of causing serious damage to the skin and hair of angora goats (Graham and Hourrigan, 1977) and considered to be a threat to the Angora fibre industry world-wide. Ivermectin injected subcutaneously (200 mg per kg body weight) is an effective method of control (Bates, 2001; Odiawo and Ogaa, 1987).

Psoroptes in horses

Equines can be infested with three species of *Psoroptes*: *P. cuniculi* (*P. hippotis*) infesting the ears and *P. equi* and *P. natalensis* infesting the body (Sweatman, 1958).

P. cuniculi has been recorded in Australia (Lucas, 1946; Johnston, 1963; Shaw, 1966; Arundel, 1978; Pascoe, 1980), Great Britain (Gerring and Thomsett, 1980), France (Henry, 1917) and the United States (Montali, 1976). A survey of horses in Queensland showed 20 percent to be infested (Pascoe, 1980). Clinical signs of equine psoroptic otoacariasis may be restricted to ear discharge, but can also include ears held at right angles or giving a lop appearance (Shaw, 1966; Montali, 1976). Ear drooping is usually associated with severe rubbing of the affected ear or ears. Other common symptoms in horses include scratching ears with the hind feet (Shaw, 1966), rubbing the ear base on stalls etc. (Lucas, 1946; Shaw, 1966; Montali, 1976), head shaking (Lucas, 1946; Shaw, 1966; Gerring and Thomsett, 1980; Montali, 1976) and touchiness of poll (Lucas, 1946).

Equine psoroptic mange (*P. equi*) has been recorded in Germany (Diez and Wiesner, 1984), Libya (Gabaj *et al*., 1992), South Africa (Zumpt, 1961), Sudan (Abu Samra *et al*., 1981; Abu Samra *et al*., 1987) and Great Britain (Kirkwood, 1986a). In Great Britain equine mange (psoroptic or sarcoptic) was notifiable, due to its economic effects on the working horse, especially during wartime, but it was deregulated in 1983, due to the decreased agricultural and military importance of the horse, and the successful use of γ BHC washes. Severe outbreaks of equine psoroptic mange occurred in Germany during the Second World War and the disease was still notifiable in both East and West Germany up until 1984 (Dietz and Wiesner, 1984).

Psoroptes on cattle

Two species of *Psoroptes* infest cattle: *P. ovis* and *P. natalensis*. *P. ovis* (the sheep scab mite) has been recorded in Argentina (Nuñez, 1989), Czechoslovakia, (Sevcikova *et al*., 1987), Belgium (Losson, 1996), India (Gill *et al*., 1989), Italy (Genchi *et al*., 1995), Libya (Gabaj *et al*., 1992) and the United States (Hourrigan, 1979). *P. natalensis* has been recorded infesting cattle in Brazil (Sweatman, 1958), France (Sweatman, 1958), India (Shastri and Ghafoor, 1974), New Zealand

(Sweatman, 1958), South Africa (Hirst, 1922), South America (Rocha *et al*., 1952), Uruguay (Sweatman, 1958) and Great Britain (Bates, 1999b).

Bovine psoroptic mange begins as moist plaques of hair over the withers, followed by intense pruritus with active rubbing against fixed equipment, leading to loss of hair, serum exudation, ulceration and bleeding. Eventually, thickened, scabby lesions, oozing blood and serum, progress over the withers and tail-head, before extending along the back and down the flanks and legs (Linklater and Gillespie, 1984). Pyoderma is common due to secondary bacterial infections. Psoroptic mange can be life threatening to calves under one year old but deaths rarely occur in older animals, although infested cattle are predisposed to pulmonary infections and may die (Losson, 1996). Like sheep scab, bovine psoroptic mange is considered a winter disease, but clinical outbreaks are sometimes observed in July or August (Losson, 1996; Hirst, 1922). Heavy infestations are readily detected, but light infestations are difficult to discern, especially during the early stages of disease, when lesions are very small (Bates, 1997; Fisher *et al*., 1986). Mixed infestations with *Chorioptes bovis* or *Sarcoptes scabiei* var. *bovis* are common, complicating control measures (Losson, 1996). Cattle mange can spread rapidly within confined situations of a feedlot but transmission at pasture is slower, especially in the summer when there is no close body contact and mites are in the ("alleged") quiescent phase (Meleney and Christy, 1978).

In Great Britain, 61.4 percent of bovine mange is caused by *C. bovis* and 30.0 percent by *S. scabiei* var. *bovis*. The remaining 8.6 percent of cases were due to isolated outbreaks of *Psoroptes* spp. imported from mainland Europe (Bates, 1997). The current low prevalence of bovine mange in Great Britain may be associated with treatment for other ectoparasites, e.g. compulsory treatment for warble fly (*Hypoderma* sp.), initially using systemic organophosphates and latterly ivermectin-based formulations. In addition, the current increase in the use of endectocides (doramectin, ivermectin, moxidectin etc.), either as anthelmintics or ectoparasiticides, may have contributed to the current low prevalence (Bates, 1997).

Bovine psoroptic mange is present on mainland Europe. In Belgium an estimated 400 000 cattle are treated each year (Pouplard *et al*., 1990). Belgian White and Blue cattle (BWB) represent around 50 percent of the Belgian national herd and are highly susceptible to *Psoroptes,* with infestations being generalized and chronic (Losson, 1996). In general, beef breeds are more susceptible and dairy breeds (e.g. Holstein) are more resistant. Bovine psoroptic mange was once notifiable in the United States and is still considered to be a major parasite of cattle.

Bovine psoroptic mange has been incriminated as the cause of a defect ("white spot") in leather, although conclusive evidence is lacking (George *et al*., 1986).

Psoroptes on sheep (sheep scab)

Sheep scab (*Psoroptes ovis*) is a form of allergic dermatitis initiated by allergens contained in the mite secretory or excretory products (Bates, 1981). *P. ovis* exploits the allergic reaction: the heat and humidity produced by the inflammation forming the micro-climate needed for mite survival and the leakage of serous exudate forming the basis of the mite's nutrition (Bates, 1981). In this inflamed condition skin breakages occur, mainly as a result of host scratching but also through small haemorrhages caused by the abrasive action of the mite's mouthparts. These skin breakages result in increased leakage of serum, with accompanying scab formation and skin thickening (Raffert and Gray, 1987).

Sheep scab can have profound effects on the health, welfare and economics of infested flocks through the effects of ram fertility (uncomfortable or interrupted mating), weak or still born lambs (through nutritional stress as a result of the constant irritation), reduced lamb growth and death of breeding stock (through debility and exhaustion, dehydration, secondary bacterial infections or hypothermia). The yield and quality of by-products such as leather and fleece are also adversely affected.

In 1986 scab was reported in at least 149 countries throughout the world (**Table 1**), with the disease still notifiable in many (Kirkwood, 1986b). Although eradicated from Australia, New Zealand and the United States, scab is considered to be a serious threat to the sheep industries of Europe, South America and southern Africa. Some Member States of the European Union have Government implemented control or eradication schemes, other states treat the disease as it occurs, having no national policy. There is a possibility therefore, that new strains of *Psoroptes ovis* could be transported throughout the Member States, particularly as a result of the Single European Market.

2 RESISTANCE DEVELOPMENT

As with other parasites, resistance to acaricides in populations of mites results from the selection of individuals with lower inherent susceptibility by exposure to acaricides. It is likely that genes that confer resistance are already present at very low levels in the parasite population before the introduction of a new acaricide. Although resistance develops slowly initially, once identified, it quickly becomes a problem. The rate at which a resistant allele becomes established in the population and the time it takes for the control of the parasite population to be lost is dependent on many factors. These include: frequency of the original mutation in the population before treatment, mode of inheritance of the resistant allele, frequency of acaricide treatment, and the proportion of a population that is not exposed to the acaricide.

Mites are obligate parasites with only small populations in refugia, so a resistant allele can become established very quickly in the population. However, the small population in refugia does enable much more efficient control of mange.

A practical definition of resistance to a given product is: “decreased susceptibility of an ectoparasite to an insecticide (or acaricide) at concentrations on or above a defined threshold”. The defined threshold concentration being the dose stipulated by the manufacturer for its use, printed on the product label (e.g. the maintenance concentration for plunge dips). Basically this means that if all the instructions are followed to the full and the product is still ineffective (following controlled investigations), the parasite can be considered to be resistant to that product (Bates, 1998). Another definition must also be considered, that of “tolerance”. Tolerance can be described as “a decreased susceptibility to an insecticide or acaricide at concentrations below a defined threshold” (usually shown by *in vitro* studies). In practical terms this can be interpreted as: “if all the manufacturer’s instructions are followed to the full and the product is still effective”. Progressive tolerance can lead to resistance.

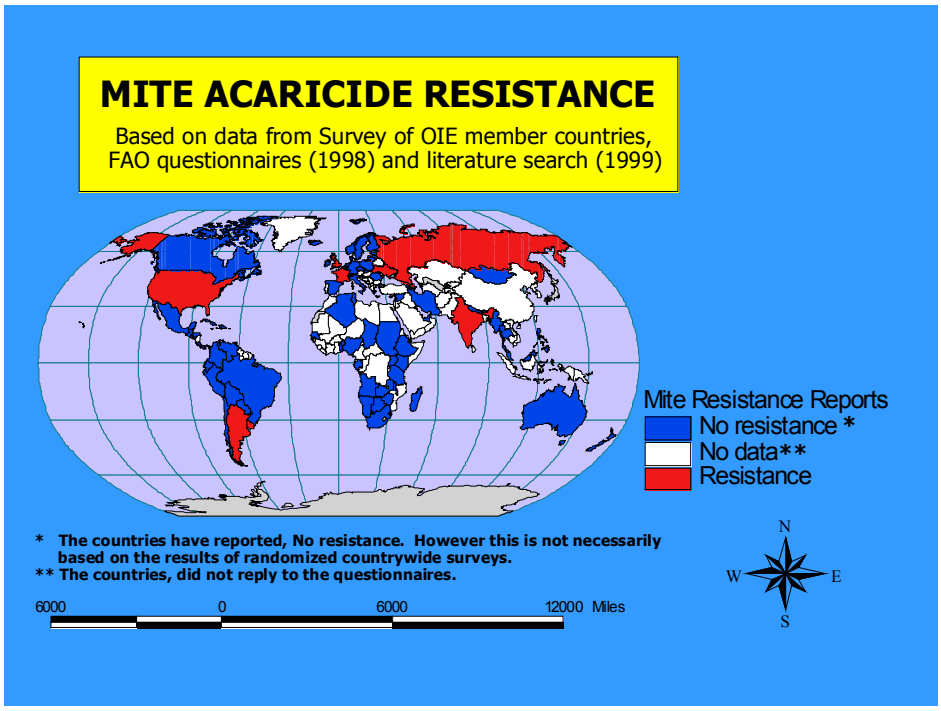
3 CURRENT STATUS

Sheep scab

Scab was eradicated from Norway in 1894 and Sweden in 1934 (Kirkwood, 1986b) and both countries continue to remain free from disease. Scab was eradicated from Denmark in 1929 (Henriksen, 1979) and continued to be free from infestation for more than 50 years until infested sheep in several flocks were confirmed in the late 1970s (Henriksen, 1979), presumably from Germany. Periodic infestations have since been recorded (Henriksen *et al*., 1995).

The recent history of sheep scab in Germany is not dissimilar to that of the United Kingdom. Scab was almost eradicated from the Federal Republic of Germany (FDR) in 1948 by plunge dipping in γ BHC, but notification requirements were not being strictly observed and infestations resurged in 1973 (Liebisch *et al*., 1978; Meerman, 1978). Whereas in the past the majority of German sheep were regularly dipped at least once a year, a certain degree of negligence developed while scab was at a very low prevalence. Many flocks were dipped every two years or even after longer intervals. A further problem was the restrictions imposed on γ BHC. A considerable proportion of the increase in sheep numbers in the FDR since 1967 (5 percent per

annum) took place on the dyke farms of the North Sea coast. In addition to the increasing demand for mutton, a further incentive to increase flock size was the additional European Commission (EC) money for sheep kept in outer dyke areas. The resultant higher stocking density, close contact and scarcity of forage were the main factors conducive to the spread of sheep scab. Another factor was the communal sheep farms (common grazing) set up in North Friesland when sheep were kept on dyke pastures in the summer (Meerman, 1978). Scab was deregulated in 1991 and responsibility for control was left exclusively to the farmer (Worbes, 1995). The expansion and liberalization of the livestock trade following the re-unification of Germany, experimentation with new breeds and the introduction of the Single Market in 1993 saw a considerable number of new outbreaks (Worbes, 1995).



Scab was notifiable in France, although the law was generally never complied with (Autef and Girard, 1987). Despite national awareness campaigns there was a lack of strictness among farmers in deciding to carry out treatment or in choosing a correct method, product or regular prophylaxis (Autef and Girard, 1987). This lack of strictness led to poor results following treatment and an increased frequency of "accidents" with considerable mortality leading to court cases, and blame put on the method or the product (Autef and Girard, 1987), although laxity has been incriminated as the main cause of failure in France (Autef and Girard, 1987). Sheep scab was deregulated in France in March 1995 (Personne, *personal communication*.), but it still remains compulsory to treat infested flocks. Scab is generally found in the areas of the country among flocks grazed exclusively outdoors and in the south of the country where transhumance is practised (several flocks gathered together in the period May to September to graze the mountains). There are local control programmes, where it is compulsory for all sheep in these areas to be treated with the help of the local veterinary services. These programmes involve 20 percent of the national flock and have shown promising results (Personne, *personal communication*).

The history of scab control in Ireland mirrors that of the rest of the British Isles, only there was no period of temporary eradication. Sheep scab is notifiable in the Republic of Ireland, but compulsory dipping was abolished in 1994. The onus or responsibility to notify scab is now with the flock owner or veterinary surgeon. While scab was eradicated from the rest of the United Kingdom, the disease was still prevalent in Northern Ireland. Scab was recorded in 272 Irish flocks at the time of removing compulsory dipping in 1993 (O'Brien, 1992). Like the majority of Europe, γ BHC was withdrawn from the Irish market in 1985 due to meat residues and environmental concerns (O'Brien, 1996).

In Great Britain scab was made notifiable in 1869, and in 1948 the organochlorine γ BHC (lindane) was approved as a single dip, but the continued use of the old double dipping formulations was allowed (Page, 1969; Spence, 1951). γ BHC dips, together with rigid official enforcement, good sheep husbandry and restricted animal movement were responsible for eradication in 1952. It was postulated that eradication was achieved, not because every sheep had been dipped, but because every infested sheep had been dipped (Kirkwood, 1986a). The continued presence of chewing lice (*Bovicola ovis*) proved this. Scab was re-introduced to Great Britain in 1973 and γ BHC based dips continued to be used until 1984, when they were voluntarily withdrawn following pressure from Europe over possible residues in lamb exported from Britain (Henderson, 1991). Organophosphate formulations containing diazinon or propetamphos eventually replaced γ BHC in the fight against scab. Since the re-introduction of scab in 1973, there were a variety of policy measures aimed at eradicating the disease for a second time (Bates, 1999b). Without Government control scab could cost the United Kingdom sheep industry £600 million over thirty years (Kirkwood, 1986a). The cost to the Government for State veterinary input was estimated to be £12 million per annum together with £2.1 million for Local Authorities to enforce Government policy. Together with this expense the question was asked, "why should scab remain notifiable?": it is easily controlled, it is not zoonotic, the compulsory use of organophosphorus (OP) based dip formulations may be an unnecessary health risk, synthetic pyrethroid (SP) based dip formulations may have a severe ecological impact, adequate animal health legislation is in position and the EU makes no mention of sheep scab. Consequently scab was deregulated in June 1992 (Anonymous, 1992). Reasons for failure to eradicate scab were identical to France, Germany and Ireland. In addition, flocks were not inspected regularly, owners were not aware of the symptoms of scab or unwilling to report disease, flocks were not completely gathered and those that were, were not dipped correctly. The growing antipathy to OP dips may also have been important (Bates, 1999b). Since compulsory annual dipping was abandoned in Britain (and the Republic of Ireland), the problem of sheep scab has received much attention (O'Brien, 1996). The infrastructure involved in these schemes, and which accompanied the relevant treatment regime, has mainly disappeared. It is now impossible to quantify the extent of spread. However it is unquestionable that there has been an increase geographically and numerically in outbreaks of the disease (O'Brien, 1996).

In Brazil scab was under control for almost 20 years, but there was a resurgence in 1976 (Kirkwood, 1986b). It is now endemic in southern Brazil and is still a notifiable disease in Argentina and Uruguay. The use of γ BHC virtually eradicated scab from Argentina by 1960 (Nuñez, 1977). Unfortunately eradication was slowed down with the development of resistant strains of *P. ovis* in 1962 (Ault *et al*., 1962). The introduction of diazinon followed with initially spectacular results, but in 1965 the efficacy of diazinon dips in the provinces of south eastern Buenos Aires was in doubt, and diazinon resistance was first recorded in 1966 (Rosa and Lukovich, 1970). The development and maintenance of resistance was observed to be directly related to the standard of animal husbandry and the relative importance given to sheep production (Nuñez, 1977). In the Province of Patagonia, where sheep were the main enterprise, the standard of husbandry was high and scab resistance was rare. In the provinces of south eastern Buenos Aires, Entre Rios and Corrientes, where sheep production was secondary to other agriculture, the

standards of husbandry were low and resistance was a significant problem (Nuñez, 1977). Falling world wool prices have forced drastic reductions in the Argentinean national flock (44 million in 1980 to 9 million in 2001) and have virtually eradicated (resistant) sheep scab in areas where mixed farming was predominant. Sheep farming is still profitable in Patagonia, where large flocks predominate and scab continues to be a problem (Olaechea, *personal communication*). Similarly the number of sheep in Uruguay has dropped to 14 million and sheep have lost their importance. In some areas farmers are unwilling to invest in disease control and these areas continue to be foci of infestation. Uruguay abandoned compulsory plunge dipping in 1997 (Bonino, Mari and Mederos, *personal communication*).

Scab has been a problem in the Republic of South Africa since the 17th century and has increased in prevalence since 1973 (Van Heerden, 1977). The disease was almost eradicated in the 1930s using lime-sulphur dips. Sporadic outbreaks between 1940 and 1966 were mostly due to unlawful sheep movements across borders, and sheep migrating from neighbouring states. Since only sporadic outbreaks occurred in South Africa for almost 30 years up to 1967, few farmers, stock inspectors and veterinarians had experience with the disease. The main market for South African wool is Germany, which, like most European Union States, is concerned about high levels of insecticide (Erasmus, *personal communication*). In 1992 the South African authorities observed the outcome of scab deregulation in the United Kingdom, contemplating mutual deregulation. At present scab is still notifiable and an increasing problem, spreading from the former tribal homelands (where common grazing is practised) and the independent territories of Lesotho and Swaziland. Since the “new government”, there has been a breakdown in official control policy and a severe reduction in extension services (Louw, *personal communication*). It is compulsory under the Diseases of Animals Act to treat all ectoparasite infestations and to have a permanent dip tank. An unsuccessful campaign was launched by the South African Government in 1990, but scab is now left for the farmer to control. Local husbandry methods make control difficult and eradication seems impossible. Scab was eradicated from Lesotho in 1935 but returned in 1973 (Kirkwood, 1986b).

4 DIAGNOSIS OF RESISTANCE

Acaricide resistance is mainly detected through field experience, after failure of a particular treatment. It must be understood that in the case of mites, proper treatment and control measures can only be implemented in conjunction with an accurate diagnosis. Failure of treatment is often difficult to detect as mites can survive on the host without showing any sign of their presence (Bates, 2000b).

There are five different methods of identifying populations of *Psoroptes* resistant to contact acaricides (organochlorines (OCs), organophosphates (OPs) or synthetic pyrethroids (SPs)), three *in vitro* methods and two *in vivo* methods. The three *in vitro* methods could also be adapted for *Chorioptes* mites. The first is based on the use of "tea bags" where mites are exposed to different drug concentrations. The bioassays principally assess efficacy by determining LC_{50} (or LC_{90}/LC_{95}) values in order to calculate a resistance factor (RF). The LC_{50} (or LC_{90} or LC_{95}) is the concentration of acaricide that is lethal to 50 percent (or 90 or 95%) of mites after correction for non-specific mortality in the negative (solvent) control. It is also important to note that when deciding suitable concentrations, dip bath concentrations of OC or OP acaricides do not equate to fleece levels (the dip bath concentration of diazinon may be 400 ppm but the levels of diazinon in the fleece may be 4000 ppm (Bates, personal communication).

5 DETECTION OF RESISTANCE: PROTOCOLS FOR RECOMMENDED METHODOLOGIES

1. Tea bag dipping *in vitro* test

The original method (Wright and Riner, 1979) has been adapted and used routinely at Onderstepoort, South Africa. A fusion of the two protocols is described below.

Filter paper or heat sealable rice paper envelopes ("tea bags") (2.0 to 5.0 cm long × 2.0 to 6.0 cm wide) are prepared. Three sides of each envelope are sealed.

Suspected acaricide-resistant mites are collected directly from donor animals, using a vacuum pump device or a mounted needle.

Under a dissecting microscope, 20 to 30 normal adult female mites are selected and introduced into the "tea bags" (immature mites are prone to escape) and the open side is sealed with a "bulldog clip".

A suitable range of dilutions of the test acaricide are prepared (**Table 2**) and maintained (in 100 ml aliquots) in aluminium foil dishes (to prevent contamination).

The envelopes are then held in forceps and dipped in appropriate concentrations of the test acaricide, for between 20 and 30 seconds, with constant stirring.

To prevent depletion of the acaricide, only one tea bag is immersed in each acaricide dilution. Replicates are also prepared.

In each case, untreated controls without exposure to acaricide are also prepared.

A separate run should also be carried out using an acaricide-susceptible population of *P. ovis*.

Envelopes are hung up to dry (at room temperature) and examined after 24 hours (Wright and Riner, 1979), or incubated in an unsealed humidity chamber (85% relative humidity (RH)) at 26°C and examined after 3 hours.

Envelopes are opened and mite mortality recorded under a dissecting microscope.

Mortality assessments are made as follows: live mites = normal movement. Dead/dying mites = immobile or unable to walk normally.

2. Slide immersion *in vitro* bioassay

A slide technique has been published for the house dust mite (*Dermatophagoides* spp.) (Mollett, 1995), although it has not been validated for *Psoroptes* (*Chorioptes or Sarcoptes*).

Twenty five adult female mites are fixed (ventral side up) onto double sided adhesive tape attached to a 2.5 × 7.5 cm glass microscope slide.

Slides are immersed in the diluted acaricide (**Table 2**) and gently agitated for 15 seconds.

The slides are then removed, and rested on one edge on filter paper at room temperature for at least 15 seconds.

They are then transferred to a humidity chamber at 25°C and 75 percent RH and mortality assessed after 48 hours.

3. Micro-titre immersion *in vitro* assays

An *in vitro* micro-titre immersion bioassay has been used in the United Kingdom since the late 1980s to screen candidate acaricides and evaluate possible acaricide resistance. A similar assay has been used in Hungary to compare the efficacy of pyrethroids against a deltamethrin resistant population of *P. cuniculi* (Pap *et al*., 1997).

Place ten active, adult female or male/female nymphal *P. ovis* into designated wells of labelled, plastic micro-titre plate using a mounted needle. Each well represents an acaricide dilution.

Using a Gilson automatic pipette, quickly transfer 150 ml of the respective acaricide dilution (**Table 2**) into the wells containing the live mites.

Cover the plate with disposable (Titertek) adhesive plate covers to prevent evaporation and the effects of solvent vaporization.

Incubate at room temperature (20°C to 25°C) for 24 hours.

Examine each well for two minutes using a dissecting microscope and record the numbers of live and dead mites.

This method has been employed at the Veterinary Laboratories Agency (VLA) (Weybridge, United Kingdom) since 1988, in parallel with animal (*in vivo*) studies. Controlled dipping of sheep infested with flumethrin resistant populations of *P. ovis* were ineffective at 33.0, 44.0 and 66.0 mg/l flumethrin, and flumethrin sensitive populations were eradicated from infested sheep at all dilutions assessed. A lethal dose of above 66.0 mg/l was therefore indicated for the resistant isolates. In comparison, micro-titre immersion assays using a formulated flumethrin dip wash demonstrated an LC_{90} of 31.72 mg/l for the flumethrin sensitive population and LC_{90}s of 78.85 and 87.79 mg/l for the flumethrin resistant populations. These results corresponded well with the *in vivo* assays. The assays initially used analytical grade flumethrin and were flawed with many technical problems. The main problem being that analytical flumethrin was extremely difficult to dissolve in any solvent that was not itself highly toxic to the mites. A commercial dip formulation containing flumethrin, and diluted in distilled water, was therefore used. The *in vitro* test using formulated flumethrin is therefore an accurate and inexpensive method of assessing for pyrethroid resistance in the sheep scab mite.

4. *In vivo* "cell test"

Healthy, full fleeced sheep, without previous treatment for ectoparasites and free of external parasites, are prepared as follows:

The wool along the dorsal area is cut off with scissors in order to expose the skin. The skin is then gently clean shaved using a scalpel blade. The animal is then rested for 24hrs.

The bottom halves of 5 cm diameter aluminium (“pill-box”) cells are then glued to the skin using Superglue® (one cell per dilution of acaricide).

Twenty five to 30 adult female mites are introduced into each cell at day 0, and the lid secured.

At day 7, the presence of mites or a lesion in each cell is confirmed.

At day 14, each cell is exposed to a particular concentration of an acaricide for 30 seconds, and the lid replaced.

The cells are then examined for live mites and resolution of the lesion at three day intervals for a total of 21 days.

Table 2. Recommended dilutions

Acaricide	Dilution (mg/l)				
γ BHC	50	100	200	400	800
Diazinon	25	50	100	200	400
Cypermethrin	50	75	100	125	150
Flumethrin	20	40	60	80	100

5. *In vivo* "control test"

Groups of healthy, full fleeced sheep, without previous treatment for ectoparasites and free of external parasites, are challenged with 25 to 30 adult female *P. ovis* obtained from donor animals.

Infestations are allowed to progress for 42 days, with a check to confirm active colonization after 7 days.

After this time, mite counts (*in situ*) and lesion measurements are recorded and the animals are treated with the product with suspect resistance, strictly according to the manufacturers recommendations.

For plunge dipping, the correct volume of water must be added to the dip bath (using a water meter) and the required volume of acaricide concentrate accurately measured and added to the water. The wash must then be thoroughly mixed for not less than five minutes. Dip wash samples must be taken after mixing and after the sheep have been dipped and the concentration of acaricide confirmed by chemical analysis (e.g. gas liquid chromatography (GLC)).

For injections and pour-ons, the syringe or pour-on/spray-on gun must be calibrated, as must all weighing equipment where acaricide administration is according to body weight.

All sheep must be examined for live mites and resolution of disease 7, 14, 28 and 56 days after treatment.

There are currently no published methods to investigate resistance in *Psoroptes* to ingested acaricides (e.g. doramectin, ivermectin or moxidectin), however methods of investigating resistance in *Sarcoptes* have been published (Brimer *et al*., 1993; Brimer *et al*., 1995). These tests are based upon the migrational ability of *Sarcoptes* mites on the surface of agar gels containing acaricide. Mite activity is expressed as a migration index (MI) and compared to a known standard. Good responses were recorded for the organophosphates (OPs) parathion, phosmet and phoxim (Brimer *et al*., 1993) and for ivermectin (Brimer *et al*., 1995). The test is accurate, sensitive and easy to carry out, but like all acaricide resistance assays, requires accurate determination of the acaricide concentration in the substrate (i.e. gel).

Standardization and interpretation of bioassays

Dilutions must be: made up on the day of assay using volumetric glassware, tightly stoppered and used within 3 hours of dilution.

Concentration of acaricide in the dilutions must be verified by chemical assay (e.g. GLC).

Mites must be used within 3 hours of collection.

If possible, bioassays should be carried out in parallel with a known sensitive or resistant isolate.

Untreated (solvent) controls must be included for each isolate of mite.

Mites will be recorded as alive if they have total mobility or active movement of two or more limbs: they will be recorded as dead if less than two limbs show active movement.

LC_{50} and LC_{90} values are calculated from the corrected mean percent mortality (i.e. data corrected for the non-specific mortality in the negative (solvent) controls) by linear regression using a programmable calculator.

Data corrected for the non-specific mortality in the negative (solvent) controls (mean corrected percentage mortality) are calculated using the formula:

$$(M_p - M_s)/(100 - M_p) \times 100$$

Where M_p = mean test product mortality (%)

M_s = mean solvent mortality (%)

Data collected from the bioassay will be valid until a mean mortality of 30 percent or above is recorded in the test product solvent control. Once a mean mortality of 30 percent or above is recorded in the test product solvent control the bioassay will be terminated.

New techniques under development: enzyme assays

Techniques have been developed measuring the amount of carboxylesterase E_4, an enzyme known to cause resistance to a wide range of insecticides in the peach-potato aphid (*Myzus persicae*) (Devonshire and Moores, 1984). A total esterase activity using the whole homogenate of a single aphid gives a quantitative measure of activity (Devonshire, 1975). This is preferable when investigating very resistant aphid populations because E_4 contributes virtually all the activity. In slightly resistant populations other esterases, common to all variants, make a large contribution and can obscure the smaller differences in the amount of E_4 between resistant and susceptible aphids. In this case electrophoretic analysis is preferable as it allows isolated E_4 to be estimated from the intensity of the stained band on the gel (Baker, 1977; Blackman *et al*., 1977). Although the activity of E_4 has been quantified in gels by spectrophotometry (Blackman *et al*., 1977) this is not practicable on a large scale. These techniques may be of use investigating acaricide resistance in mange mites.

Glutathione-S-transferases (GSTs) have been identified in 24 insect species as a polymorphic protein occurring in up to eight isoenzymes in some cases (Baker *et al*., 1994; Yu, 1996). GSTs are used by insects and mites to metabolize xenobiotics in the body (Capua *et al*., 1991; Ibrahim and Ottea, 1995) and elevated levels of GSTs have been shown to confer insecticide resistance (Yu, 1996; Ibrahim and Ottea, 1995; Prapanthadera *et al*., 1995; Bond and Bradley, 1997; Hemmingway *et al*., 1997) in a wide variety of medical, veterinary and agricultural pests. At present there are no published techniques for quantifying the amounts of GSTs in parasitic mites.

6 EPIDEMIOLOGY

The epidemiology of sheep scab

The prevalence of sheep presenting scab lesions within infested flocks can vary between 7.8 and 60.0 percent in large flocks, and the prevalence of sub-clinical lesions (i.e. lesion areas below 100 cm^2 or 2.5% body cover) can be between 10.0 and 90.0 percent. Sub-clinical disease is generally asymptomatic; symptoms if they do occur include occasional episodes of restlessness, rubbing against fence posts etc., soiled and stained areas of wool (particularly on the shoulders), head tossing and deranged or tagged fleece. Differential diagnosis can be problematic as these symptoms are also indicators of the presence of other ectoparasites (e.g. chorioptic mange, chewing lice *(Bovicola ovis*), blowfly myiasis (*Lucilia* spp.), keds (*Melophagus ovinus*), biting

flies, or even scrapie. It is of paramount importance that the cause(s) of flock irritation are identified. Administration of an inappropriate control strategy may select for acaricide resistance.

The sheep chewing louse (*B. ovis*) is a common parasite of sheep on common grazing uplands of the United Kingdom. Sheep with pre-disposing infestation of chewing lice will not accept challenges of sheep scab mites, whereas sheep with active scab can be colonized by lice following natural exposure. The exact nature of this inter-species exclusion is unknown, but the skin changes initiated by lice feeding/excretion may render it unfavourable for mite colonization. Lice, on the other hand, may actively feed on the scab lesion (Bates, 1999c), particularly after administration of an endectocide has eradicated *P. ovis.*

In the later stages of *Psoroptes* infestations, rubbing and head tossing become more evident and areas of wool loss appear together with open, bleeding wounds. Sheep rapidly lose condition and epileptiform seizures may be evident (Bygrave *et al*., 1993). Numbers of infested sheep within the flock can vary from one or two in the early days of infestation, to the whole flock as the disease takes hold (depending on the immune status of each individual sheep). Throughout the flock there will be animals with non-established lesions (that will eventually die out) and young sub-clinical lesions, together with animals with obvious extensive disease. All sheep should be considered to be infested and the whole flock should be treated for scab. One missed sheep could re-infect the whole flock.

The transmission of scab is through direct contact between sheep or indirectly, through contact with residual mites in tags of wool or scab attached to fencing, etc. Although *Psoroptes* spp. mites are obligate parasites, they are still capable of surviving off the host for 15 to 16 days (O'Brien *et al*., 1994a), before succumbing to starvation and desiccation. An infestation can be initiated by only one egg laying female or hundreds of mites, depending on the mite burdens on other infested sheep or in the environment, together with the relative period of contact. Infestations can spread rapidly through lowland flocks with restricted grazing but may be slower through extensively grazed hill flocks, that are thinly spread over common grazing and infrequently mustered (Kirkwood, 1986a). Scab outbreaks in Britain originated from lateral spread from contiguous flocks, strays etc. (33.9%), movement of sheep via market (22.3%), direct sheep movements (15.9%) and persistent infestations on unenclosed land (1.0%). Although this direct transmission was the predominant method, an element of indirect transmission is present in all outbreaks, i.e. via mites deposited at marts, in livestock lorries etc. Although the origins of the outbreaks were fully explained in over 73 percent of cases, the origins of infestation remained obscure in 18.5 percent of flocks and disease recrudesced in 0.7 percent of flocks (Bates, 2000b). The development of acaricide resistant strains of *P. ovis* during this period was not suspected.

Sheep scab is a winter disease, with the majority of cases in the Northern Hemisphere occurring between September and April, although a significant number of cases do occur in the summer months, particularly on animals still full fleeced (lambs, hogs etc.) and on "ridges" of longer fleece on poorly shorn sheep. These sheep can subsequently infest ewes with an adequate fleece length. Sheep scab mites were once thought to migrate to the "cryptic sites" (the ears, the infra-orbital fossae, the inguinal pouches and the crutch) in order to survive the summer ("latent phase" or "suppressed scab") (Downing, 1936; Spence, 1949). The migration of *P. ovis* to the cryptic sites is not in dispute, but the intentional seasonality of the migration is open to question. *P ovis* can be found in the cryptic sites of sheep with extensive disease, and then more often in the winter than the summer (Kirkwood, 1986a). Mites have been recorded in only 7 percent of sheep with detectable infestations in one or more cryptic sites during the summer compared to mites over-summering on the broad body surfaces of 32 percent of sheep examined (Roberts *et al*., 1971).

Two species of *Psoroptes* have been recorded to infest sheep: *P. cuniculi* infesting the ears and *P. ovis* infesting the body (Sweatman, 1958). In Great Britain *P. cuniculi* has been recorded

within tubes of scab situated within the last centimetre of the external auditory canal (EAC), next to the tympanic membrane, from sheep with no recent history of scab (Bates, 1996a; Bates, 1996b). Symptoms of psoroptic otoacariasis differ between lambs and adults. In adults the symptoms ranged from the asymptomatic to aural haematomata, violent head shaking and ear rubbing, leading to excoriation and wounding of the ear and ear base. In lambs symptoms include plaques of scab (often bloody) on the external ear cleft, excoriation of the ear base, ear scratching with the hind feet and inflammation of the external aspects of the horizontal canal. In all cases the internal pinnae are clear of the typical psoroptic scabs characteristic of mites in the cryptic phase. *P. cuniculi* ear mites are morphologically identical to the sheep scab mite (*P. ovis*), but do not initiate clinical scab on transfer to scab naive sheep and are not therefore reservoirs of infestation.

On the other hand *P. ovis* were observed in the EACs of 38.6 percent of infested sheep presenting lesion areas from 20.9 to 100.0 percent body cover (Bates, 1999b). Although the incidence of *P. ovis* otoacariasis increased as the leading lesion edge approached the ears, 20.0 percent of sheep were infested in the EAC when the leading edge was as far away as the mid-back. In studies investigating the temporal progression of sheep scab it was demonstrated that *P. ovis* migrated to the EAC as early as 28 days following artificial challenge, with the leading edge 28.0 cm from the base of the ears (Bates, 1999b). Unlike *P. cuniculi*, *P. ovis* isolated from the EAC can be infective to the bodies of sheep. Acquired resistance to scab may have a direct effect on the growth of sheep scab lesions originating, if aural *P. ovis*, (or residual body mites in the regressed or cryptic phase of infestation) are to re-infest their previously infested host (Bates, 2000c). Colonization would be more successful on scab naïve hosts.

Long periods of latency and a sudden increase in vigour and pathogenicity of a mite strain could account for unexplained outbreaks of disease (Roberts and Meleney, 1971). Distinct populations of *P. ovis* were identified in the United States, varying in population reduction in the summer, tolerance to OP acaricides, survival off the host and relative rate of spread through cattle herds (Roberts and Meleney, 1971). Similar studies have been carried out in Great Britain (Bates, 1999d). All the geographical isolates of *P. ovis* which were compared produced a progressive lesion, characteristic of sheep scab, but the extent of the lesion produced with time varied considerably between the isolates (Bates, 1999d). Some created slow chronic infestations while others produced fast acute infestations over the same time period.

7 CURRENTLY AVAILABLE CONTROL STRATEGIES

The decision as to which method of scab control to use depends on government policy, the size of the flock, the age of the sheep, whether the sheep are pregnant or lactating, the use to which they will be put (meat, wool, milk or breeding), the availability of labour and facilities (handling pens, dip baths, etc.), weather, geography and the presence of other parasites (nematodes worms, lice, ticks, keds and blow flies) (Bates, 1993). The acaricides currently used for the control of sheep scab (and cattle and pig mange) are shown in **Table 3.**

The currently available tools for mange control consist of chemical technology, relying on treatments with different application methods and/or formulations of acaricides. These can be used with or without the benefit of local epidemiological knowledge.

Farmers and veterinarians implement treatments against mange most commonly when the disease is evident. According to the epidemiology, mange is primarily a winter disease, with the majority of cases in the Northern Hemisphere occurring between September and April, and in the Southern Hemisphere between April and July. Highly effective treatments such as those given during the “cryptic phase” using macrocyclic lactones, are a very good strategy for eradicating mange because they eliminate the source of infection for the next season.

Table 3. Acaricides used for the control of sarcoptic, chorioptic and psoroptic mange

Acaricide	Application	Mite genus	Host
Abamectin	Injection	Psoroptes, Sarcoptes,.	Cattle (National Office of Animal Health, 2000)
Amitraz	Sprays/washes	Sarcoptes	Pigs (National Office of Animal Health, 2000)
		Sarcoptes, Chorioptes, Psoroptes	Cattle (Curtis, 1985)
	Pour-on	Sarcoptes	Pigs (National Office of Animal Health, 2000)
	Plunge Dip	Psoroptes	Sheep (Muñoz Cobenas *et al*., 1978)
γ BHC	Wash/Spray	*Sarcoptes*	Pigs (Tucker and Cutler, 1982)
		Sarcoptes, Chorioptes, Psoroptes	Cattle (Schwardt, 1949; Lancaster and Meisch, 1986)
	Plunge Dip	Sarcoptes, Chorioptes, Psoroptes	Sheep (Spence, 1951)
Coumaphos	Plunge Dip	*Psoroptes*	Sheep (Lancaster and Meisch, 1986)
Deltamethrin	Plunge Dip	*Psoroptes*	Sheep (Personne, personal communication)
	Shower Dip		
	Jetting		
Diazinon	Plunge Dip	*Psoroptes*	Sheep (Kirkwood and Quick, 1981)
Doramectin	Injection	*Sarcoptes*	Pigs (National Office of Animal Health, 2000),
	Pour-on	Sarcoptes, Psoroptes	Cattle (National Office of Animal Health, 2000)
		Sarcoptes, Chorioptes, Psoroptes	Sheep (Bates *et al*., 1995; McKenzie, 1997)
			Cattle (National Office of Animal Health, 2000)
Eprinomectin	Pour-on	Sarcoptes, Chorioptes. Psoroptes	Cattle (National Office of Animal Health, 2000)
Fenvalerate	Plunge Dip	Psoroptes	Sheep (Personne, personal commmunication)
	Shower Dip		
	Jetting		
Flumethrin	Pour-on	Psoroptes	Cattle (Losson and Lonneaux, 1992)
	Plunge Dip	Psoroptes	Sheep (Kirkwood and Bates, 1987)
Moxidectin	Pour-on	Sarcoptes, Chorioptes, Psoroptes	Cattle (National Office of Animal Health, 2000)
	Injection	Sarcoptes, Psoroptes	Cattle (National Office of Animal Health, 2000) Sheep (Parker *et al*., 1999)
High-cis Cypermethrin	Plunge Dip	Psoroptes	Sheep (O'Brien *et al*., 1997)
Ivermectin	Injection	Sarcoptes	Pigs (National Office of Animal Health, 2000)
		Sarcoptes, Psoroptes	Cattle (National Office of Animal Health, 2000), Sheep (O'Brien *et al*., 1993)
		Sarcoptes	Pigs (National Office of Animal Health, 2000)
	In-feed	Sarcoptes, Chorioptes Psoroptes	
	Pour-on	Sarcoptes, Chorioptes, Psoroptes	Cattle (National Office of Animal Health, 2000)
	Bolus		Cattle (National Office of Animal Health, 2000) Sheep (Bridi *et al*., 1998)
Permethrin	Pour-on	*Chorioptes*	Cattle (National Office of Animal Health, 2000)
Phosmet	Pour-on	*Sarcoptes*	Pigs (National Office of Animal Health, 2000),
		Sarcoptes, Chorioptes, Psoroptes	Cattle (National Office of Animal Health, 2000) (Meleney and Roberts, 1979)
Phoxim	Spray	Psoroptes	Cattle (Hourrigan, 1979)
	Plunge Dip	Sarcoptes, Chorioptes, Psoroptes	Sheep (Muñoz Cobenas *et al*., 1978; Meerman, 1978)
Propetamphos	Plunge Dip	Psoroptes	Sheep (Kirkwood and Quick, 1982)

The impact of acaricides on the environment and as residues in food is a continuing concern. The dependence on chemicals to control scab mange and other parasites is under continual review.

Four control alternatives are used:

1. Suppressive (systematic or eradication) treatments.
2. Ad hoc or opportunistic treatments.
3. Curative treatments.
4. Strategic treatments.

1. Suppressive treatments towards eradication

Suppressive treatments are carried out for eradication purposes.

Principle: Treatments against mange are applied at short intervals (twice every 9-12 days) to eliminate completely all the parasitic stages. All animal introductions must be treated immediately upon arrival in order to avoid the spread of new mites onto the farm.

Prerequisites: These include a sustainable supply of inexpensive acaricides and the necessary infrastructure and animal health and production services. In cases where the strategy is used for the eradication of mites, the following would also be required. A long-term commitment that involves thorough epidemiological surveillance, obligatory periodic acaricide application, adoption of quarantine procedures, adequate training for personnel and the active participation and co-operation of farmers, legal support of the respective governments, and adequate, long-term guaranteed financial resources. Extensive knowledge of biological aspects of the mites and the participation of adequately trained personnel are further essential structures for successfully achieving such a goal. Such campaigns are ultimately dependent upon the continued chemical efficacy of the products employed, or their successful substitution. Ongoing monitoring of acaricide efficiency is therefore crucial. Once eradication is complete, there is usually some form of physical border to be maintained between the mange-free and the mange-infested areas. Administration of such borders will be an expensive and long-term requirement.

Advantages: Although eradication of mange from a prescribed area remains a daunting and expensive task, if achieved and maintained, the long-term benefits are generally compensatory.

Disadvantages: Delays in the process of mange eradication could lead to acaricide resistance due to the extended intensive exposure to chemicals.

Epidemiological consequences: Risks of acaricide resistance.

Possible combination with other strategies: Highly effective treatments given during the "cryptic phase" using macrocyclic lactones, are an effective strategy for eradicating mange, because they eliminate the source of infection for the next season. All oncoming stock should be quarantined for at least three weeks, and observed for signs of infestation. If a given area or country does not meet the necessary prerequisites, eradication should not be promoted.

2. Ad hoc or opportunistic treatments

Principle: In connection with general management practices (weaning, dehorning, change of pasture or paddocks) farmers often implement routine preventive procedures and antiparasitic treatments. On some occasions they may use macrocyclic lactones that will have acaricidal effects as well as anthelmintic activity. It is usual that farmers decide when the animals should be treated according to their own estimates of "economic thresholds" for mite infestation, time available, climatic conditions, availability of personnel, acaricide and basic infrastructure.

Prerequisites: No special requirements need to be met.

Advantages: There is a reduced overall need for gathering animals, resulting in a reduced input of human and economic resources.

Disadvantages: Due to the biological cycle of mites, only one opportunistic treatment may be inefficient and results are unpredictable when assessed solely from the perspective of immediate mange control. The effectiveness of this strategy in reducing mite populations is questionable, as the interval between two opportunistic treatments is often too long (>10 days) for the acaricide to prevent the completion of the mite's parasitic development on the host.

Epidemiological consequences: The effective reduction of overall mite population is doubtful. Reinfection from mite eggs not affected by the treatment, could maintain the disease on the farm.

Possible combination with other strategies: Regular clinical observation to avoid the sudden spread of the disease.

3. Curative treatments

Principle: Farmers implement curative treatments when some animals are presenting clinical signs of mange and/or whenever the risk of production losses and/or uncontrolled disease is considered to be significant.

Prerequisites: The presence of a regularly applied monitoring system such as clinical examination.

No other special requirements need to be met.

Advantages: Only those animals with clinical signs are treated. There is a reduced overall need for gathering all animals on the farm, resulting in a reduced input of human and economic resources.

Disadvantages: The approach is usually inefficient in the long term because the disease is maintained on the farm. Reinfestation will occur. Due to the biological cycle of mites, only one curative treatment may be inefficient and results are unpredictable when assessed solely from the point of view of immediate mange control.

Epidemiological consequences: The effective reduction of overall mite population is doubtful. Reinfestation from mite eggs not affected by the treatment can maintain the disease on the farm.

Possible combination with other strategies: Treated animals should be observed for signs of clinical evolution and if feasible, kept isolated from the remaining animals.

4. Strategic treatments

Principle: Farmers implement strategic treatments in the early autumn, before there is an increase in the number of mange outbreaks, and during summer when animals are suffering from just subclinical mite infestations.

Prerequisites: All animals should be treated. All introductions should be observed clinically, to avoid the introduction of infested animals in the farm.

Advantages: Because animals are infected by a low number of mites, early autumn treatments remove the mite population and there will be no mange outbreaks during this season. Removing mange during the summer season means that no further mite infestation will appear in the next season.

Disadvantages: There is a need for gathering all animals on the farm, resulting in an increased input of human and economic resources.

Epidemiological consequences: There will be effective control of mange on the farm.

Possible combination with other strategies: All introductions should be treated in order to avoid introduction of "new" mites onto the farm.

8 CHEMICAL CONTROL

Inorganic compounds

The early control of scab was based upon plunge dipping in one of four active ingredients: tar acid/tar oil dips, arsenic dips, lime-sulphur dips and tobacco dips, all of these requiring a second dip within 14 days to kill emerging eggs (Spence, 1951).

Organochlorine (OC) compounds

The next group of insecticides to be developed were the organochlorines and cyclodienes, e.g. γ BHC, aldrin and dieldrin. The mode of action of OCs was not clearly understood, but they were known to destroy the delicate balance of sodium and potassium within the cell, thus preventing normal transmission of nerve impulses. From 1945 onwards, plunge dip formulations were developed containing γ BHC. These were effective at a single dipping, eradicating scab and lice, together with sufficient chemical remaining on the fleece and skin to kill hatching parasites for a considerable number of weeks after dipping (Spence, 1951). Dichlorodiphenyltrichloroethane (DDT) or dieldrin were not effective against *P. ovis* (Nuñez, 1977), although they were highly effective against lice and blowfly (*Lucilia* sp.) larvae. Dieldrin and DDT were withdrawn from the United Kingdom market in the late 1960s, primarily on environmental grounds. Up to the mid 1980s, plunge dipping in γ BHC wash was the major acaricide in the war against scab world-wide, and continued to be used in the United Kingdom until 1984, when it was voluntarily withdrawn due to residues in meat (Nuñez, 1977). Strains of *P. ovis* resistant to γ BHC were reported in Argentina in 1962 (Ault *et al*., 1962), hampering scab control (Nuñez, 1977). During the eighteen years of compulsory use against sheep scab in the United Kingdom, no cases of γ BHC resistance were recorded. Eventually scab control changed to the use of organophosphate based formulations (Kirkwood, 1986a).

Organophosphate compounds

The organophosphate based plunge or shower dip formulations were the next generation of insecticides to appear on the market. OPs act by inhibiting cholinesterase (ChE) enzymes and by preventing the removal of acetylcholinesterase (ACh). The latter "jams the circuit" through its accumulation and interferes with the neuromuscular junction. Diazinon was approved for scab control in the United Kingdom in 1981 (Kirkwood and Quick, 1981), although it had been licensed for blowfly and lice control since the early 1970s. Propetamphos was approved for scab, lice and blowfly control in the United Kingdom in 1982 (Kirkwood and Quick, 1982). In France plunge dipping is considered effective for large flocks. Full fleeced sheep are immersed for 60 seconds and shorn sheep for 30 seconds, with the head pushed under twice. In the United Kingdom and Ireland all sheep are immersed for 60 seconds regardless of fleece length.

OP dip formulations began to be incriminated in post-dipping illness in stock owners and contractors (Anonymous, 1989b). Consequently, safer insecticides were investigated for their efficacy against scab, lice and blowfly strike.

Synthetic pyrethroids (SPs)

In 1987 the first non OP dip, containing the synthetic pyrethroid flumethrin, was licensed in the United Kingdom for scab and lice control (Kirkwood and Bates, 1987a), and ten years later high-

cis cypermethrin (HCC) was licensed for the British market (O'Brien *et al*., 1997). Flumethrin is not licensed for scab control in France or the Republic of Ireland. SPs have the advantage of excellent selectivity and high toxicity to arthropods and relative safety to mammals. SPs affect the neuronal membrane, modifying the sodium channels, probably impeding protein conformational changes at the lipid-protein interface, in a manner similar to OC compounds. SPs have remarkable similarities with DDT. Both DDT and SPs have two types of insecticide effect, a) initial rapid knockdown (Kd), rendering the insect motionless and b) a subsequent lethal effect. Development of resistance to DDT by pests around the world was thought by many to foreshadow a similar fate for the SPs (Miller, 1988). The biggest advantage of SPs is that they can also be formulated as pour-ons, revolutionizing louse control on sheep (and cattle), particularly in Australia.

During the years of compulsory dipping in the United Kingdom there was no suspicion of OC, OP or SP resistance. There was in fact little chance of resistance developing in either obligate parasite, *Psoroptes* or lice, due to the "overkill" nature of compulsory dipping, which also included the supervised "double dipping" of confirmed scab infested flocks, and the strict government control of insecticides on the market. Dip formulations containing diazinon, propetamphos or flumethrin were "approved" before the deregulation of sheep scab in 1992. Approval was granted only if they cured the disease and provided protection from re-infestation for at least three weeks on shorn and unshorn sheep. Approval of intermittent replenishment dips was based upon the lowest concentration likely to occur under field conditions (i.e. the maintenance level) (Kirkwood and Bates, 1987b), and was set well below the initial make up concentration and well above the minimum lethal concentration. The maintenance level for non-stripping dips (e.g. flumethrin) is close to the make up concentration, but in stripping dip formulations (e.g. OP) the make-up concentration is considerably higher. The maintenance concentrations for flumethrin, diazinon or propetamphos were 44 ppm, 100 ppm and 125 ppm respectively. The initial make up concentration and the maintenance concentration in the non-stripping flumethrin dip are more or less equal.

OP (propetamphos) and SP (flumethrin) resistant strains of *P. ovis* emerged in Great Britain after deregulation, and to dip formulations that were scab approved during the eradication campaign. Deregulation also removed the requirement for the approval of dip formulations and supervised dipping, resulting in the potential for ineffective treatment. In 1994 two populations of *P. ovis*, from two geographically isolated areas (southwest England and northern Scotland) were found to be resistant to a flumethrin based dip at the recommended use rate of 44 ppm, and also at the stronger rate of 66 ppm used for tick control (Syng *et al*., 1995). Following the identification of these two isolates, a further two flumethrin resistant strains were identified in 1995, both originating from northeast England (Clarke *et al*., 1996). All these isolates were confirmed resistant after extensive laboratory dippings at the VLA (Weybridge). These were the first confirmed cases of acaricide resistance in *P. ovis* in Europe. Further populations have subsequently been shown to be resistant to flumethrin by field investigations and the problem appears to be widespread. In the winter of 1995, a strain of *P. ovis* isolated from northern Scotland, was confirmed resistant to the OP propetamphos after controlled dipping at the VLA (Weybridge) (Bates, 1998; Clarke *et al*., 1996).

Amitraz has been shown to be effective against *Psoroptes* (*Sarcoptes* and *Chorioptes*) (Curtis, 1985; Muñoz Cobenas *et al*., 1978) but dip formulations are not currently licensed in the United Kingdom for scab control, although they are licensed in South America, South Africa and mainland Europe. Although effective against scab, they are very expensive and only used as "OP resistance breakers" and the dip wash has to be stabilized in the dip bath using calcium hydroxide. Cheaper generic amitraz products are now available. The OP sebacil (phoxim) is

licensed in Europe (not the United Kingdom or the Republic of Ireland) for scab control (Meerman, 1978; Worbes, 1995).

Psoroptes mites are known to colonize deep within the ear canals of sheep, and dip wash containing a blue dye did not penetrate the ear canal completely (Bates, personal communication). Mites in the ears could therefore survive dipping and their exposure to sublethal concentrations of acaricide could select for resistance.

SP plunge dips are, in general, more effective than pour-on formulations. This is not only because of their acaricidal effect, but also because they physically wash the scab lesion. Since the deregulation of scab in 1992, stockowners (particularly those suffering from the toxic effects of OPs) were no longer obliged to use plunge dips and were confronted with a wider choice of products for the control of ectoparasites. SP pour-ons are not effective against sheep scab (Bates, 1993) and their routine use in the United Kingdom for the control of lice, ticks, blowfly or headfly, could have induced resistance to SP dips, or even augmented existing SP tolerance within a population (Bates, 1998). The belly and legs cannot be reached by pour-on formulations, thus increasing the probability of mite survival.

Systemic injections

Macrocyclic lactones (MLs) are fermentation products of soil micro-organisms and have been chemically modified to produce the avermectins (ivermectin and doramectin) and the milbemycins (moxidectin), with greater potency and broader spectrum anti-parasitic activity than their fermentation precursors (abamectin and nemadectin, respectively). The first endectocide to be licensed for scab control was ivermectin (derived from *Streptomyces avermitilis*), with two subcutaneous injections given seven days apart (Bates and Groves, 1991; O'Brien *et al*., 1993; Soll *et al*., 1992). Unfortunately it offered little or no residual protection against re-infestation, therefore sheep must not be returned to infested pens/pastures for at least 17 days. In September 1997 another avermectin, doramectin, was licensed for scab control and was curative after a single intramuscular injection (Bates *et al*., 1995; McKenzie, 1997). Noticeable failures to doramectin have been recorded in France, where it is administered as a single subcutaneous injection at 200 μg/kg (Personne, personal communication). In the United Kingdom it is administered as an intra-muscular injection at the higher rate of 300 μg/kg. Although the recommendations for doramectin in Europe only require one injection, two injections are required in Argentina. Studies in neighbouring Uruguay have demonstrated that a single, intra-muscular injection of doramectin at 200 or 300 μg/kg was 100 percent effective in controlling artificial infestations of sheep scab (Cardozo *et al*., 2000).

Single or double subcutaneous injections of the milbemycin, moxidectin (derived from *Streptomyces cyaneogriseus*) have been shown to cure scab and to provide residual protection against reinfestation for 28 days (O'Brien *et al*., 1994b; O'Brien *et al*., 1996; Williams and Parker, 1996; Parker *et al*., 1999). Moxidectin does not possess the disaccharide side chain (present in all the avermectins) and has unique side groups: a methoxine group and a dimethylbutenyl group. These subtle differences in molecular structure give rise to markedly different pharmacokinetics and potency properties of moxidectin compared to the avermectins. MLs are referred to as "endectocides" being effective against both internal (endo-) parasites and external (ecto-) parasites. Their main advantage over plunge dipping is that they are quicker and safer to use, cause less stress to the sheep (including pregnant ewes), do not require any special handling facilities and fixed equipment (i.e. dip baths) and there are not the same environmental concerns over the disposal of spent products (Bates, 1993). They also have the added advantage that they are effective broad-spectrum anthelmintics. Their main disadvantage is their relatively narrow range of efficacy against ectoparasites, and alternative compounds may be required for the control of lice, ticks and blowfly. They also require a relatively long meat withdrawal period

(Bates, 1993). Because sheep scab is a form of allergic dermatitis, sheep can suffer irritation for some time after eradication of *P. ovis* by MLs (Bates and Groves, 1991).

In Argentina the availability of over 40 relatively cheap, generic, ivermectin based products has led to injection surpassing plunge dipping in popularity, with grave concerns regarding the selection for ivermectin resistance. Many farmers have now broken up their dipping facilities, relying solely on the use of endectocides. In the United Kingdom and South Africa there is an increasing problem with chewing lice (*Bovicola ovis*), through the sole use of endectocides for scab control.

Long acting formulations of ivermectin, effective after single injection (at 300mg/kg), are licensed in Argentina (but not currently in the United Kingdom). Ivermectin is still detectable 30 to 35 days after treatment, but withdrawal periods are less of a problem for wool growers.

Ivermectin has also been studied as an intra-ruminal controlled release capsule (CRC). Complete eradication of *P. ovis* was achieved within 28 days of administration with protection against re-infestation for 21 to 28 days (Bridi *et al*., 1998).

In the United Kingdom single subcutaneous injections of ivermectin (200 μg/kg) failed to eradicate artificial infestations of a moderately virulent population of *P. ovis*. Mite numbers were reduced by 52 percent within 24 hours, 90 percent within 10 days and 96 percent within 20 days, but live mites were still detectable 86 days after treatment (Bates and Groves, 1991). The numbers of surviving mites correlated directly with the mite burden at the time of treatment (Bates and Groves, 1991). Moulting (pharate) mites cannot feed, consequently they may only ingest sub-lethal concentrations of acaricide once they are active. Potential for this evasive strategy therefore increases proportionally with mite population at the time of treatment (i.e. the virulence of the population). Differences in the efficacy of single injections of ivermectin with respect to mite virulence were thus observed (Bates, 1994). Low virulence populations (characterized by low mite numbers) can be almost eradicated after a single injection, yet significant numbers of mites survive within high virulence populations (characterized by high mite populations). Double injections however eradicated all populations of sheep scab mite (National Office of Animal Health, 2000).

Oral drenching with ivermectin produced a 48 percent drop in mite numbers within 24 hours of treatment, but there was little further decline and no relationship between the initial mite burden and the extent of control (Bates and Groves, 1991). The apparent inefficacy of oral ivermectin may have significant effects on the epidemiology of sheep scab by extending the sub-clinical phase, or selecting for resistance to other endectocides administered by injection (e.g. doramectin, ivermectin or moxidectin).

9 APPLICATION METHODS

The choice of formulation and method of application of the acaricide naturally depends on the size of the farm and the management system. Small-scale farming operations facing mange problems might achieve control by using spray or pour-on formulations. Medium and large farms with more facilities and equipment, might use immersion dips or injectable formulations. In-feed preparation for pigs and boluses for cattle, are other alternatives. An ideal acaricide should be economically acceptable, easily applicable and should have good efficacy with sufficient residual effect to protect animals from re-infection. It should not select for resistance due to its gradual decay on the animal (i.e. it should have a sharp cut-off in efficacy with time). In addition, it should have a minimal toxicological effect on animals and man, with only minimal residues in meat and milk. Unfortunately, such an ideal acaricide has not yet been produced.

Plunge dips

Plunge dips remain one of the most efficient and reliable methods for routine acaricide applications at farm level.

Advantages: With this procedure, the animals is completely wetted, all parts of the body having adequate contact with the acaricide solution.

Disadvantages: Problems with maintenance of the correct concentration of the acaricide are common. Elaborate installations for handling of animals are necessary. There can be environmental pollution from the run-off liquid when the animals emerge from the dip. The facilities are expensive to build. They are not appropriate for some acaricides (such as MLs) for stability and other reasons.

Wash/Spray

Application of acaricide to sheep and cattle can be carried out using various modes of spray devices, e.g. spray races or corridors, motorized pumps, backpack manual pumps.

Advantages: If carried out correctly, animals receive more individual treatment; the amount of the acaricide applied is controlled and the concentration of the acaricide is adequate. Spraying is also generally less expensive per head than dipping, and the chemical group can easily be changed. No stabilizer is required for amitraz if it is used immediately.

Disadvantages: The animals are not always completely wetted, especially in the lower body parts, insides of the ears, etc. Animals must be appropriately secured during the operation. With the backpack manual pump, it is time-consuming and fatiguing for the operator. The use of manual spray pumps may well be the simplest method of acaricide application to animals, but not necessarily the most effective. Its success depends very much on the operator's skills and the effectiveness of restraining the animals. There is the risk of environmental pollution. There is increased risk of intoxication to the operators. There are frequent problems with blocking of the spray nozzles.

Pour-ons

The introduction of this method of acaricide application was a remarkable advance in technology for applying acaricides. A volume of the acaricide proportional to the weight of the animals is applied along/on the dorsum of the animal, from where it dissipates over its body surface to kill infesting mites. In the case of some SPs (depending on their residually active period), they could also offer continuing lethal and repellent protection against subsequently arriving mites. In the case of ML compounds, the method permits the parasiticide to be absorbed and to act systemically.

Advantages: Acaricides are easy to apply. Environmental pollution is reduced. It is a very practical method, especially where no dip tanks are available, or in circumstances when the producer wishes to avoid dipping some of the infested animals (e.g. pregnant females, just a few animals need to be treated, etc.). Some of the SP compounds can be applied with this formulation. New formulations of MLs and other compounds employing this method of application are being introduced onto the market and offer an alternative for the control of pyrethroid resistant strains of sheep and cattle mite.

Disadvantages: The higher cost of these new compounds may be an initial limitation for many farmers in developing countries. High concentrations of the applied chemicals are needed for good efficacy. There are currently no pour-on formulations available for the control of sheep scab.

Injectable formulations

This is another practical alternative to avoid the dipping or spraying of animals with acaricides. Most of the injectable products currently on the market are the MLs.

Advantages: There is reduced environmental pollution, except possibly in the dung pats where non-target species may be affected. There is a broad spectrum of action (against endo and ectoparasites). They also provide alternative acaricides for the control of pyrethroid and amitraz-resistant strains.

Disadvantages: Possible residues of such products in milk restrict their use in dairy animals. In general terms, these compounds are more expensive than the other alternatives.

10 NON-CHEMICAL CONTROL

Alternative control strategies including vaccines and biological control are unlikely to be widely available in the near future and even when they are, they will be integrated with chemotherapy (Hennessey and Andrew, 1997).

11 CONTROL STRATEGIES UNDER DEVELOPMENT

Action by national agricultural departments

To assure the success of any control programme, resistance testing is necessary before deciding which pesticide should be used and resistance monitoring needs to be continued during the campaign (Thullner, 1997). The frequency of resistance monitoring activities will depend on the parasite's generation interval (Thullner, 1997).

Regional or national veterinary authorities, local veterinary surgeons, agricultural extension services and farmers' groups should be informed if resistance has been identified in their localities. This will allow the situation to be monitored and if required, the correct alternative treatments to be prescribed.

The laboratory carrying out or responsible for resistance testing should be recognized by the regional or national authority concerned. The same laboratory should be responsible for resistance monitoring (Thullner, 1997).

A standard methodology for resistance diagnosis should be defined and agreed upon by all parties involved. A definitive standard operating procedure (SOP) should be prepared that is compliant with an agreed quality scheme (e.g. Good Laboratory Practice (GLP)).

This quality scheme should include a definition of the susceptible reference isolate (Thullner, 1997) and should be low cost and unsophisticated, but validated at regular intervals by a central laboratory using more sophisticated methods.

The maintenance of a susceptible reference strain is required (Thullner, 1997) and should be maintained according to an agreed SOP at the recognized laboratories.

The risk of cross-resistance needs to be covered within the context of efficacy testing. This requires the nomination of resistant strains (Thullner, 1997), again maintained according to an agreed SOP at the recognized laboratories.

A scheme for monitoring resistance development after product registration should be defined.

Action by research institutes.

In addition to reliable resistance testing and monitoring, there should also be investigations into resistance mechanisms and their development. This will allow resistance risk analyses to be carried out in the future (Thullner, 1997).

Research efforts must concentrate on the better use of existing insecticide technology (optimizing treatment times, understanding the resistance status of the target pest, etc.) (Levot, 2000).

Investigations into the host specificity of ectoparasites and possible refugia from treatment is necessary.

Action by regulatory authorities

The cornerstone for sustainable pesticide resistance management (PRM) is the consideration of the resistance issue in pesticide registration requirements. This should cover proper pesticide use, resistance diagnosis and monitoring and preventative measures (Thullner, 1997).

A scheme for monitoring resistance development after product registration should be defined.

The diagnosis of resistance in non-target species through intensive use of a product should be a consideration at registration.

Consideration should be given to the method of product application. The easier this is, the more effective the product is likely to be in the field.

The actual regulations for the registration of veterinary products should be considered. In the United Kingdom prior to 1992, all dips etc. requiring scab approval had to be 100 percent effective against sheep scab. This also conferred 100 percent efficacy against chewing lice. After the deregulation of scab in 1992, the European Commission stipulated in 1974 that only 95 to 98 percent efficacy was required for the licensing of ectoparasiticides. What happens to the two to five percent of the parasites not susceptible to the treatment?

Methods of testing the efficacy of ectoparasiticides for registration should be standardized using an agreed SOP.

Action by the farmer

Strategies should be based on Integrated Pest Management (IPM) techniques, exploiting the biology of the pest, reducing selection pressure to a minimum, increasing the useful life of a pesticide and decreasing the interval of time required for a parasite to become susceptible once more to a given pesticide (National Research Council, 1986).

Insecticides should only be used if absolutely necessary and an annual “blanket treatment” of the whole flock should be avoided.

Rotation, alternation or sequences of different classes of parasiticide or different modes and sites of action to control the same parasite are accepted as valid strategies to avoid resistance (National Research Council, 1986). Do not use an SP dip if an SP pour-on is routinely used for the control of other ectoparasites.

Where there is no refuge for the population exposed to the insecticide there is a high selection pressure. This is extremely important in the case of permanent parasites such as mites or lice.

Treatment of uninfested animals is undesirable.

Reduce the use of insecticides.

All oncoming stock should be quarantined for at least three weeks (21 days), observed for signs of infestation and only treated if an ectoparasite has been diagnosed. If an ectoparasite is suspected, a veterinary surgeon should be consulted to advise correct treatment.

If ectoparasites are suspected, the parasite should be professionally identified to ensure that only a product licensed for the control of that parasite is administered, and administered correctly.

Quarantined animals should not be mixed with the main flock until treatment is complete and the parasite eradicated.

In an area where resistance has occurred, continued use of a pesticide may be required to control other parasites which remain susceptible. This could confound attempts at parasite management. In the United Kingdom, SP pour-ons have in the past been used for the control of ticks (*Ixodes ricinus*) in upland grazing (also where scab and lice are currently a serious problem). Use of macrocyclic lactones as anthelmintics (employing injections, oral dosing or slow release boluses) may select for resistance in ectoparasites. The use of OP or SP plunge dip formulations administered through shower dips or jetting races may also select for resistance.

Using doses that are less than 100 percent effective may reduce the threat of resistance if low levels of the parasite can be tolerated (Kunz and Kemp, 1994), i.e. meat producing sheep and chewing lice.

The excessive use of parasiticides for short-term gains may be the worst possible practice in the long term (Kunz and Kemp, 1994).

Fewer or less frequent applications, which reduce the selection pressure over time, would decrease the rate and probability of resistance development (Kunz and Kemp, 1994).

Apply existing products effectively and according to the manufacturer's instructions and using "Good Treatment Practice" (Bates, 1999e). Attention must be paid to the maintenance of plunge dips and showers. The capacity of the dip bath or sump must be accurately calculated and recorded, as should any drop in volume in relation to replenishment. Attention should be applied to top ups and replenishment.

Not all insecticides or their methods of application are effective against all ectoparasites (i.e. broad spectrum). The parasite infesting the flock must be professionally identified and the correct, licensed treatment administered (and administered correctly). The routine use of SP pour-ons for the control of lice, ticks, blowfly or headfly, could have induced resistance to SP dips, or even augmented existing SP tolerance within a population.

Ectoparasites have relatively short generation times, producing relatively large numbers of offspring per generation. The product label instructions must be carried out. If the label states two treatments, then two treatments must be administered. The first treatment will only kill the active stages of parasite present on the sheep at the time of treatment. The second treatment will kill any eggs that have hatched since the first treatment.

Once the sheep are mixed with the main flock the buildings/paddocks housing the infested sheep must be thoroughly cleaned and disinfested with a suitable insecticide. All litter and discarded wool must be collected and burnt or deposited out of sheep contact. No sheep should be housed/grazed in the disinfested area for at least 21 days.

12 RESISTANCE MANAGEMENT AND INTEGRATED CONTROL

The development of resistance to current chemical classes of insecticide/acaricides presents an undeniable threat to the long-term viability of the animal health industry (Hennessey and Andrew, 1997). The significant cost of research and development of new therapeutics for food producing

animals, together with the small market share of animal health products is a positive disincentive for drug development. The chemical actives currently available are all that we are likely to have for the foreseeable future, and they must be used more effectively (Hennessey and Andrew, 1997). Insecticides available to producers will probably be "lost" at a greater rate than the registration of new compounds (Levot, 2000). If concerns over residues mean that consideration is given to deregistration or further regulation of pesticide use, producers must be provided with alternative control strategies (Levot, 2000). Rational pest control strategies are needed to manage resistance, not only to prolong the effectiveness of current pesticides, but also to reduce the environmental impact of these substances (Kunz and Kemp, 1994).

Although efforts to establish integrated pest management (IPM) are increasing, control and eradication campaigns still depend largely or totally on pesticides, and can therefore be jeopardized by pesticide resistance (Thullner, 1997). Pesticide resistance triggers a chain reaction which, through deteriorated efficacy, leads to more residues and finally becomes an obstacle to world trade, particularly when maximum residue levels (MRLs) are exceeded (Thullner, 1997). It is often assumed that survivors do not receive a lethal dose and farmers may react by increasing the dosage or frequency of application, resulting in further resistance of susceptible parasites and an increase in susceptible individuals (Kunz and Kemp, 1994). This irrational countermeasure can lead to increased residues in meat, milk, wool or hides, together with the environmental impact of processing the latter. When this happens the next step is to switch to a new product, and with the same type of persistent application, resistance to the new chemical evolves in the same way (Kunz and Kemp, 1994).

Pesticide safety issues

Pesticide safety is multifactorial and includes: consumer safety (meat/milk residues); operator safety (human poisoning); environmental safety (eco-toxicity) and safety to the target host species.

Operator safety is of paramount importance in pesticide approval in the United Kingdom. Repeat exposure to low levels of OP may lead to delayed toxicity. Genetic differences may contribute to differences in individual toxicity. In 1993 the purchase of OP dips was restricted to those holding a ‘Certificate of Competence’. The use of SP dips in the United Kingdom increased in parallel with their misuse and, together with the loss of disease investigation and supervision of dipping with the deregulation of sheep scab, the first cases of SP resistance began to appear.

In 1997 there was an upsurge in water pollution incidents (mainly with SP) associated with sheep dipping, particularly in Wales and the north of England. In 1998 the Certificate of Competence Scheme was extended to include SP dips. Farmers wishing to dispose of sheep dip onto land that might lead to a direct pollution incident also had to apply for a licence. Farmers then turned to the endectocides for scab control.

MODULE 4 REFERENCES

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