Breeding for Resistance to Infectious Diseases of Small Ruminants in Europe

L. GRUNER AND F. LANTIER

ABSTRACT
Recent studies of the susceptibility to helminth infections of sheep and goats have focussed on artificial infections of lambs, kids and adults with several nematode species. Intra-breed studies have been orientated towards the elaboration of methods to investigate resistance acquired by lambs after natural or artificial monospecific or mixed infections with Teladorsagia circumcincta and Haemonchus contortus. Repeatability, heritability and correlations between types of infection (natural versus experimental) and between resistance to different species have been estimated. Possible use of blood parameters to complement faecal egg counts has also been investigated. Genetic studies on the resistance of sheep against intracellular bacterial diseases have concerned the identification of genes involved in the control of sheep salmonellosis. One of those genes could be the equivalent of the mouse Ity/Bcg/Lsh gene(s) that control susceptibility to murine infections with Salmonella, Mycobacterium and Leishmania respectively. Research in the United Kingdom has increased our knowledge of the role of the PrP protein in the susceptibility of sheep to scrapie and its role in related diseases of other animal species and humans. Research on resistance and immune responses of sheep to infectious and parasitic diseases in Europe is considered important because the sheep is an important livestock species and because it is a model species for ruminants and even for humans.

Europe is characterised by high ecological diversity caused by variable climate: from 'Atlantic' climate in the western part to 'Continental' in the East; and from 'Sub Polar' in the North to 'Mediterranean' in the South. Further diversity is caused by the presence of mountain chains and both humid and dry plains. There is a high diversity of small ruminant breeds which are specialised for meat, milk and wool production. Management systems are also highly diverse.

Small ruminant systems of production commonly are based on pasture and therefore parasitic diseases caused by helminths are of primary importance. Adults are treated with anthelmintic between one and three times per year and up to four times in young animals, to control gastro-intestinal nematodes. Commonly, young animals are treated each year to control cestodes and
Breeding for Resistance to Infectious Diseases in Small Ruminants

coccidia. Fascioliosis and dicrocoeliosis are also important; and protostrongylo­
losis occurs in goats and sheep in the Mediterranean areas.

Strains of nematodes that are resistant to anthelmintics have developed in
France, Germany, Holland, Switzerland and the United Kingdom. Resistance to the benzimidazoles is predominant, but the true prevalence of
resistance in farms is poorly documented. Recent evidence confirms that this
phenomenon is increasing in Holland (Borgsteede et al. 1991) and the
United Kingdom (Jackson 1993).

The need to reduce the use of drugs has also involved interest in
alternative and complementary methods of control such as increasing genetic
resistance to nematode parasites (Cabaret and Gruner 1988; Gruner and
Cabaret 1988; Gruner 1991; Stear and Murray, 1994). Investigations in
Europe on genetic resistance have concerned resistance to two important
nematode species, _Teladorsagia circumcincta_ and _Haemonchus contortus._

Intensive production systems for lambs include indoor management where
the main parasitosis is coccidiosis, with associated diarrhoea and loss of
production. Control measures include management and prophylactic
medication (Gregory 1989), but investigations are orientated towards charac­
terisation of common antigens from different species for vaccination. Very
little is known about the genetic resistance of small ruminants against these
diseases.

In most European countries bacterial diseases caused by intracellular
bacteria have probably the highest incidence of all infectious diseases. They
induce direct losses through abortion of ewes and does, septicemia and
pneumonia in lambs and kids (for example, _Chlamydia_, _Brucella_, _Salmonella_
and _Listeria_) or through the more specific lesions induced by _Listeria monocy­
togenes_ (encephalitis), _Corynebacterium pseudotuberculosis_ (caseous
lymphadenitis), or _Mycobacterium paratuberculosis_ (chronic enteritis). Their
increasing economic importance stems from their effects on humans, which
is linked mainly to their transmissibility through contact with livestock and
consumption of milk and meat.

Control of the most important infectious diseases is orientated towards the
development of vaccines and efficient preparations are used against brucellosis
(Plommet et al. 1987), salmonellosis (Pardon et al. 1990a, 1990b) and chlamy­
diosis (Souriau et al. 1988). Investigations on the genetic resistance of sheep to
intracellular bacteria such as _Salmonella_ have been initiated in France, with the
objective of finding a major gene for resistance. An additional aim is to increase
our knowledge of the immune mechanisms involved in resistance to intracel­
lular bacteria in ruminants and to demonstrate the feasibility of genetic
improvement of innate resistance to such pathogens of worldwide importance.
Emerging viral diseases in sheep and goat are Maedi Visna and Caprine Arthritis Encephalitis caused by lentiviruses. Studies have been undertaken in diagnosis research, epidemiology and vaccination.

Scrapie is a widespread disease with genetically determined susceptibility. It has been studied since the sixties in the United Kingdom and more recently in France. A gene for susceptibility has been determined (Hunter 1992) in mice and sheep. The mechanism of transmission of the disease and the nature of the infectious agent are largely unknown. Because of the spread of this kind of disease in Europe (and the Middle East) and the value of the work done by different teams in the United Kingdom, it seemed important to us that a short description of the current investigations should be included here.

Resistence to Parasites

The breed component of resistance to nematode parasites

European sheep breeds have been studied in the United States in comparisons between exotic and local breeds naturally infected while grazing (Stewart et al. 1937; Scrivener 1967; Loggins et al. 1965; Knight et al. 1973). In every case, the local breed was more resistant than the imported one. Comparisons of breeds for their susceptibility to natural infections (Euzeby et al. 1961), or to a single dose of Trichostrongylus axei (Ross 1970) or H. contortus (Altaif and Dargie 1978) were performed with a small number of animals. Hence it could not be concluded that the observed differences were due to breed or to a sire effect.

More recently, investigations on genetic resistance have been carried out as part of a program to increase the value of poor lands in the south of France by increasing lamb production. Experimental flocks of purebred, highly-prolific Romanov sheep, and Romanov crossbred with the local Lacaune or Mérinos d’Arles breeds, were established. These different genotypes were developed in various ecological situations to collect information on their productivity and adaptability. Animals were infected naturally and, later, experimentally with T. circumcincta. Romanov ewes were more susceptible than Lacaune ewes (Gruner et al. 1986) and more susceptible than Mérinos and crossbreds (Gruner et al. 1992a). In this last experiment, individual egg counts of the 250 ewes from the flock were performed at the end of the grazing season for four years to allow for the effects of year of sampling and the age and physiological state of the ewes. From this work, great interest has been shown in crossbred ewes which combine high prolificacy due to Romanov genes and intermediate resistance to adverse conditions including parasitosis due to heterosis (Bouix et al. 1992).
Breeding for Resistance to Infectious Diseases in Small Ruminants

In comparisons of the Saanaen and Alpine dairy goat breeds from north-western France, a significant breed effect was demonstrated for gastrointestinal nematodes and for the small lungworm *Muellerius capillaris* as measured by egg and larval outputs. In these studies faecal egg excretion was found to be lower in Alpine goats (Cabaret and Anjorand 1984; Cabaret et al. 1989; Richard et al. 1990).

**Resistance: a dynamic process of regulation of the worm population**

The breed effect described above was observed in adult animals after natural infections, but not in young kids less than 3 months old (Richard and Cabaret 1993) or young lambs (Gruner et al. 1994), after a single infection with *T. circumcincta*. This confirms that resistance is not innate. The first manifestation of regulation of the worm population was observed in these young lambs when they received a trickle infection and were slaughtered after a month when most of them had immature worms. Another manifestation of resistance was the lower proportion of worms remaining two months post infection in Merino compared with Romanov lambs. Establishment of worms was, on average, 54% of the larval dose used to infect the animals. By comparison, the establishment in adult ewes 2–7 years old, dewormed before receiving a challenge dose of 20 000 infective larvae of *T. circumcincta*, was 13% with a part of the worm burden staying at the 4th larval stage (Gruner 1991). The distribution of the worms between the animals also changed from a normal in lambs to a negative binomial in adults in which 80% of the total worms were in 20% of the infected animals. In the comparisons between Saanen and Alpine goat breeds, the conclusion was that the egg output after similar infections was greater in the Saanen breed, but the worm burden was similar; the difference was due to the prolificacy of the female worms (Richard et al. 1990).

In conclusion, resistance acts on the establishment of the infective larvae, on the rate and speed of development into the adult stage, on the survival of the adults and on the prolificacy of the female worms.

**Measurement of Resistance**

Resistance is a dynamic process of parasite regulation by the host and the faecal egg production is one of the variables which reflects this regulation. There is a need to define the type of infection and the most informative faecal egg count (FEC) which will most accurately reflect resistance. Scottish Blackface lambs with high or low FEC after natural exposure to gastrointestinal strongyles had patterns of egg output with or without a rapid peak after a challenge infection with 50 000 L3 of *T. circumcincta*, suggesting
different mechanisms of regulation (M.J. Stear, pers. comm.). Since it is not practicable to perform the high number of FECs needed to define such patterns on a large number of animals, the most informative FECs must be selected. For example, after experimental infection of Hungarian Merinos with \(H. contortus\), the best time to sample the lambs was around 50 days after a second infection (Kassai et al. 1990). Similar results were observed in Romanov sheep (Luffau et al. 1990).

**Genetic parameters**

To measure the genetic parameters of repeatability, heritability and, eventually, genetic correlation between two traits, different methods of calculation and of experimental design are available. This is illustrated by two current experiments, one in France and the other in Poland (summarised in Table 1).

**Resistance against** \(T. circumcincta\) **in Romanov sheep**

Heritabilities and their standard deviations (sd) were compared for different experimental designs, with different numbers of animals and for different values of heritability. It was concluded that the least expensive experimental design in time and number of animals necessary was bidirectional selection on one generation (Gruner et al. 1992b). This was chosen in the French experiment, to estimate the parameters of resistance to \(T. circumcincta\). The objective was to test the feasibility of a selection for resistance to natural

### Table 1  Characteristics of the French and Polish experiments to determine genetic parameters of resistance to gastrointestinal nematodes in sheep.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>France</th>
<th>Poland</th>
</tr>
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<tbody>
<tr>
<td>Breed</td>
<td>Romanov</td>
<td>Polish long wool type</td>
</tr>
<tr>
<td>Parasite</td>
<td>(T. circumcincta)</td>
<td>Predominantly (T. circumcincta) and (H. contortus)</td>
</tr>
<tr>
<td>Breeding structure</td>
<td>Bidirectional selection</td>
<td>Progeny testing</td>
</tr>
<tr>
<td>Number of animals</td>
<td>200 lambs/generation (6–10 months)</td>
<td>200 lambs aged 4–7 months (and their dams) each year from 12 sires</td>
</tr>
<tr>
<td>Type of infection</td>
<td>Natural on a contaminated pasture Experimental infection with 20000 L3</td>
<td>Natural from May to September</td>
</tr>
<tr>
<td>Faecal egg counts</td>
<td>3 x 3 times</td>
<td>Ewes 3 and lambs 2 times</td>
</tr>
</tbody>
</table>
Breeding for Resistance to Infectious Diseases in Small Ruminants

infection by using experimental infections. Two hundred male lambs, representing the maximal diversity of sires (n=21) from the same flock, were divided into two balanced flocks. One flock grazed on pasture contaminated with *T. circumcincta*, whereas the other was experimentally infected with the same strain of *T. circumcincta*—20 000 L3/lamb on three occasions separated by a treatment (fenbendazole) with three weeks of recovery time before the new dose. The lambs were between six and ten months old. Egg counts were performed three times during the 4th week post-infection and simultaneously in the grazing flock. After the last egg count, lambs were classified on the previous six counts and, in each flock, the five with highest and five with lowest index (mean root square of the six last EPG) were selected and mated with non-selected ewes. Fifty offspring of each of these four groups of males were designated the parental generation. Thus, it was possible to estimate the heritability of resistance to natural infection, the heritability to experimental infections and the genetic correlation between these two traits.

Two types of problems were encountered in natural infections. First, parents ingested a total of L3 estimated at 18 000 because of the summer drought in 1990 whereas lambs ingested around 180 000 L3 (ten times more), because of the rainy summer in 1992. Second, the difficulty of maintaining a monospecifically infected pasture obliged us to use, for the second year of experiment, a pasture previously grazed by cows the preceding year. Thus, lambs received mixed infection with *Cooperia oncophora* at a low level and eggs and individual cultures needed identifying.

Resistance in Polish long wool type sheep

This work was initiated in a selection flock of a local breed that had exchanges of sires with production flocks in the area (Nowosad et al. 1992). Each year, around 15 sires were tested in the experimental farm for production traits. Their progeny, born in February, grazed from June until the beginning of October. Individual egg counts were performed in August and September for the lambs and in May, July and September for their mothers. On each occasion in the first year, the egg counts were repeated after one week. Repeatabilities between these counts were very high and this second sample was not taken in the second year. Advantage was taken of this reduced work load by doubling the numbers of animals in the second year.

Preliminary results of these experiments (Table 2) demonstrated higher values of repeatability between the two or three egg counts done the same week after natural infection compared with the rapid evolution of the egg production of *T. circumcincta* after artificial infection. Repeatabilities between
Table 2  Preliminary estimates of the genetic parameters of resistance against gastrointestinal parasites in Romanov and Polish long wool sheep.

<table>
<thead>
<tr>
<th>Breed</th>
<th>Romanov</th>
<th>Polish long wool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animals</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Experimental Lambs</td>
<td>Natural Lambs</td>
</tr>
<tr>
<td>Repeatability of FEC</td>
<td>Year 1</td>
<td>0.42</td>
</tr>
<tr>
<td>within periods</td>
<td>Year 2</td>
<td>0.69</td>
</tr>
<tr>
<td>Repeatability of FEC</td>
<td>Year 1</td>
<td>0.26</td>
</tr>
<tr>
<td>between periods</td>
<td>Year 2</td>
<td>0.48</td>
</tr>
<tr>
<td>Heritability</td>
<td></td>
<td>0.55a</td>
</tr>
<tr>
<td>(h^2±S.E.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic Correlation</td>
<td></td>
<td>&gt;0.90</td>
</tr>
</tbody>
</table>

*See explanation in text.*

periods were lower. The within-period repeatabilities reflected the same worm population; the between-period repeatabilities reflected seasonal variations of worm population after natural infection and the new population established after the challenge dose in experimental infections. The realised heritability after experimental infections was 0.55. Drought during the parental generation in natural conditions of infection did not permit good classification of the sires as resistant or susceptible, but the estimation of the resistance of their offspring in the two types of infection suggests that the genetic correlation is very high. To confirm these preliminary results, a second generation is running with the offspring of sires selected after natural infection. In Polish long wool sheep, a heritability of 0.28±0.16 was calculated with a sire model from data of 336 offspring of 25 sires. This value was close to the estimates of Baker et al. (1991) and Watson et al. (1986) in natural mixed infections. Data from the third year of experiment will permit a more accurate estimate.

One important aspect is the relationship between FEC and worm burden. In the experiments on resistance of Romanov sheep against *T. circumcincta*, 30 lambs were slaughtered in each generation from each of the flocks with natural or experimental infections. In every case, the best correlation was between total worm burdens (or female worm burdens) and the egg counts taken close to time of necropsy, after square-root transformation. In the parental generation, larval intake during natural infection was low and the correlation coefficient was 0.80 indicating a slower turnover of the worms.
Breeding for Resistance to Infectious Diseases in Small Ruminants

Associated parameters

In Scottish Blackface and Finn Dorset, Altaif and Dargie (1978) concluded that homozygous Hb A-type sheep were more resistant to a dose of 10000 L3 of *H. contortus* in terms of FEC and worm burdens, but this was not true with a dose of 50000 L3. More recently, Kassai et al. (1990) found Hb A-type Merino sheep to be less susceptible and confirmed the relation between Hb type and the severity of anaemia. In an experiment with Romanov sheep constructed to verify the relationship between acquisition of resistance to *H. contortus* and Hb type (Luffau et al. 1986, 1990), it was concluded that faecal egg counts were not related to haemoglobin polymorphism, but might be affected by one or several genes located in the OLA complex. In this work, a statistically significant effect (P<0.05) of the haemoglobin allele received from the sire on the packed cell volume was found; it seemed that animals carrying the HbA allele were less anaemic than the others. These differences could be due to differences in oxygen affinity between HbA and HbB animals.

Stear and Murray (1994) found that resistant sheep have high eosinophil, globule leucocyte and IgA plasma cell responses with low worm burdens and that susceptible sheep have high IgG1 responses and high worm burdens. These authors concluded that the three measures of egg counts, plasma pepsinogen and peripheral eosinophilia permitted a better estimate of the worm burden of *T. circumcincta* than egg counts alone, after a challenge dose of 50000 L3.

Stability and specificity of resistance

When estimating acquired resistance it is important to account for both fixed influences on variation such as sex and breed and environmental factors that can also influence resistance. In the comparison of the susceptibility of Romanov and Méridos d'Arles ewes (Gruner et al. 1992a), the breed effect was significant in dry ewes but disappeared in ewes with one suckling lamb and the hierarchy of resistance was reversed in ewes with twins. This demonstrated the effect of the lactation intensity on the removal of the acquired resistance to gastro-intestinal nematode parasites. A benzimidazole treatment before a challenge dose has been shown to modify the expression of resistance of sheep to *H. contortus* by reducing immunity (Benitez-Usher et al. 1977; Luffau et al. 1990).

Without good knowledge of the mechanism of resistance, it is difficult to know the extent of the protection. In Romanov and Merino ewes naturally infected by grazing irrigated pastures contaminated with numerous helminth species, Merino ewes were less infected with *Nematodirus* spp., *Dictyocaulus*
Filaria, Chabertia ovina, the group formed by T. circumcincta and Trichostrongylus colubriformis and by Moniezia spp. than Romanov and crossbred ewes. Dicrocoelium dendriticum was similarly present in the three genetic types. On the other hand, Romanov ewes were infected with Fasciola hepatica and with the dominant species of the small lungworm Neostrongylus linearis (Gruner and Cabaret 1988).

Phenotypic correlations have been estimated in sheep selected against T. circumcincta and challenged with T. colubriformis (J. Bouix, pers. comm.) and in sheep selected against H. contortus and challenged with T. colubriformis (Streter and Kassai 1993). No genetic correlations between resistance against these important parasite species have been estimated but, as they often exist in the same area in Europe, with seasonal variations in their predominance, these estimates need to be made.

Genetic resistance to coccidiosis

Very little information is available on the genetic resistance of small ruminants to coccidiosis. In an experiment with 120 three-month-old lambs, faecal oocyst counts were performed over short (4 days) or longer (1 month) periods. Repeatabilities were higher in short periods and it was concluded that the component in variation of oocyst counts was similar to that recorded for trichostrongylid egg counts (Yvore et al. 1992). In a survey on 1100 lambs from 59 sires, using 2 to 3 oocyst counts per lamb, heritability estimates were between 0.10 and 0.20 (Bouix et al. 1992).

Resistance to Infectious Diseases

Resistance criteria

Usefulness of studies on innate resistance to infectious diseases has been discussed by a number of classical veterinary pathologists claiming that selection for resistant flocks might increase the number of infected individuals. In fact, genetic resistance might have more interesting consequences for the population geneticist or the epidemiologist than a 'simple' decrease in the expression of clinical signs of illness. Like good vaccines, natural resistance might also decrease the level of infection of the individuals and the excretion of the infectious agent, limiting the spread of the disease and further contamination of domestic animals and humans. So the criteria of resistance have to be carefully defined and will be preferably quantitative rather than 'death or survival' after an experimental challenge. As in laboratory rodents, the number of organisms colonising the spleen, the liver, or other target organs of ruminants can be such a criterion (Lantier and Fensterbank 1985; Lantier 1987; Pépin et al. 1991).
Breeding for Resistance to Infectious Diseases in Small Ruminants

Moreover, studies on genetic resistance to infectious diseases have focussed on pathogens against which we have imperfect means of control, or no means at all. These include microbial pathogens such as Brucella, Salmonella, Mycobacterium, or Listeria, that are able to survive in the environment and to persist for long periods in most wild and domestic mammalian hosts. Limiting the spread of such diseases, for example by increasing the resistance of the small ruminants population by genetic selection, would be of great interest.

Immunology of the sheep

Kinetic studies of the immune response during infection might provide useful immunological correlates of the host susceptibility. By using the now classical procedure developed by Biozzi et al. (1980) in mice, Amlid et al. (1980) have selected for several years in Norway two lines of goats with low and high antibody responses to antigens (heterologous erythrocytes and tetanus toxoid).

In humans, high antibody response to Mycobacterium leprae is associated with an increased severity of the disease. We have made similar observations in mice and sheep experimentally infected with Salmonella abortusovis, both for the cellular and the humoral components of the immune response (Bernard et al. 1993). Simple measurement of the antibody response after vaccination with a live vaccine might provide a useful tool for developing an experimental selection of lines resistant, or susceptible, to Salmonella or other intracellular bacteria.

The breed component of resistance to bacteria

There is breed effect on susceptibility to caseous lymphadenitis provoked in sheep by Corynebacterium pseudotuberculosis. The Prealpes breed from south of France was susceptible and the Ile-de-France breed, from the northern part of the country, was resistant. Experimental infection with C. pseudotuberculosis of groups of 20 lambs from these two breeds raised with artificial milk in absence of contamination and in the same building provided some evidence of such a breed effect on the severity of the lesions and on persistency of the challenge strain into the host (Pépin et al. 1988). However, neither breed was homogenously resistant or susceptible, and this suggests unequal frequencies of the corresponding alleles in the tested groups. The intermediate level of infection at slaughtering of F1 between Prealpes and Ile-de France (40 sheep) suggested a polygenic control of susceptibility to C. pseudotuberculosis. This remains to be tested in a second generation cross between resistant and susceptible animals.
A survey of the susceptibility to *Salmonella abortusovis* of seven French sheep breeds was made by subcutaneous challenge of groups of approximately 20 lambs with a virulent strain \((2.5 \times 10^9 \text{ S. abortusovis per lamb})\). Lambs were five-month-old males from salmonellosis-free flocks. They were slaughtered at the peak of infection, on day six, after infection and the level of bacterial colonisation were determined in organs and lymph-nodes. A breed effect was observed on a number of clinical and bacteriological parameters and on antibody responses. However, a considerable intra-breed variability was also noticed in all breeds on most measured parameters (Lantier et al. 1989). Such intra-breed variability can be used to measure the genetic parameters of the inheritance of susceptibility to salmonellosis in sheep and/or to look for the role of a major gene (see below).

**Genetics of resistance to intracellular bacteria**

In the mouse, genetic control of susceptibility to *Salmonella typhimurium* has been well established (review by Wakelin and Blackwell 1988). At least six distinct host genes are presently identified. The early growth of *S. typhimurium* in spleen and liver of infected mice is influenced by one major gene, the gene *Ity* (Plant and Glynn 1979). Gene(s) with the same localisation on mouse chromosome 1 determine the evolution of *Leishmania* (Lsh, Bradley et al. 1979) or *Mycobacteria* (Bcg, Gros et al. 1981) infections. Such gene(s) should have economic and health importance for domestic animals. Our laboratory has undertaken a series of experiments to study the feasibility of using genetic resistance to control infectious diseases in sheep (Lantier et al. 1989). Genetic control of mouse resistance to *S. abortusovis* infection has been investigated as a first step in our attempt to transpose mouse results to sheep.

*S. abortusovis* is an ovine adapted serotype which induces abortion and, to a lesser degree, mortality of young animals (Pardon et al. 1990b). *S. abortusovis* is non pathogenic for other domestic animals and humans, although it does multiply in experimentally infected mice (Pardon and Marly 1979).

Although the differences are sometimes less definitive than with *S. typhimurium*, infection of mice with *S. abortusovis* provides an interesting model. In this model, the innate mechanisms of resistance to bacterial multiplication are very likely controlled by genes similar to the ones described earlier with more classical models of *Salmonella* infection. Both humoral and cellular mechanisms are involved in innate or acquired resistance to salmonellosis. They can be investigated with the *S. abortusovis* model (Guilloteau et al. 1993) and, because the mouse experimental infection is close to the one obtained in the natural host (Lantier 1987), transposition of mouse results to sheep should be facilitated.
Breeding for Resistance to Infectious Diseases in Small Ruminants

Comparison of the levels of infection in spleen and liver of mice from various inbred lines suggested that the *Ity* gene also controlled mouse resistance to *S. abortusovis*. This was confirmed by Mendelian analysis, i.e. by testing the co-segregation of various genetic markers and of the susceptibility to *S. abortusovis* in backcross mice from resistant and susceptible mouse lines (Oswald et al. 1992). The availability of strains of mice congenic for the *Ity*/*Bcg/Lsh* region further allowed to confirm the localisation of the *S. abortusovis* resistance gene close to and very likely identical with, the *Ity* gene on mouse chromosome 1.

This region of mouse chromosome 1 has been shown to be conserved in human and bovine species and we decided to test for its conservation in sheep. By using sheep–hamster somatic hybrid lines, various markers of mouse chromosome 1 and human chromosome 2q were assigned to the sheep synteny group U11 (Tabet-Aoul et al. 1992).

The effects of this gene on the sheep resistance to *S. abortusovis* infection, or to infection with other *Salmonella* serotypes, or other intracellular pathogens of sheep, remain to be investigated. However, the demonstration of the conservation of a large fragment of chromosome (Womack and Moll 1986) raises the possibility of approaches similar to the one described above, that is to investigate similar 'genetic control of host resistance to infection and malignancy' (Skamene 1985) in mouse models of infection and in domestic animal species. The conservation of the NRAMP gene and associated markers in sheep demonstrates the feasibility of such an approach.

**Resistance to scrapie**

Scrapie is a fatal disease of sheep and goats (Hunter et al. 1992; Wood et al. 1992) involving a progressive degeneration of the central nervous system. The incubation period may last for months or years (Hunter 1992). Scrapie is transmitted by both the horizontal and vertical route by an unconventional organism, the nature of which remains the object of multiple hypotheses and discussions (Bradley and Matthews 1992). Similar diseases affect other species such as cattle, mink and cats, which are supposed to have been contaminated by infected sheep meat used for animal nutrition. Transmission of the disease from animals to humans remains highly speculative. However, progressive spongiform encephalopathy is a common characteristic of the three human diseases, Creutzfeldt-Jacob disease (CJD), Gerstmann-Strausler-Scheinker (GSS) syndrome and Kuru. More recently, fatal insomnia has also been attributed to the accumulation of prion protein (PrP) in the central nervous system (Goldfarb et al. 1992).
The PrP is coded by the PRNP gene on human chromosome 20 and mouse chromosome 2. In cattle, this gene has been recently assigned to the cattle group of synteny U11 (Womack 1993). The PrP can be isolated from the lymphoid organs (lymph-nodes, spleen) and from the nervous system in the normal host, but its role is unknown. PrP accumulates as amyloid fibrils in the organs (essentially in the brain) before clinical signs of the disease appear. Transgenic and 'knock out mice' for the PrP gene have been produced. Knock out mice normally live and are resistant to the disease, affording more evidence for the essential role of the host PrP. The genetics of resistance to scrapie has been reviewed by Hunter (1992).

Transmission of the disease from sheep to sheep, or to laboratory animals is possible by most inoculation routes (intracerebral, parenteral, oral, conjunctival) through the administration of homogenised organs (usually brain). Several 'strains' of scrapie have been differentiated by their origin, clinical signs and duration of the incubation period in inbred lines of mice. Early experimental studies of transmission of scrapie in sheep suggested a breed effect and a large intra-breed variability, in the susceptibility to the disease. Three flocks have been bred in Britain for their susceptibility and/or resistance to scrapie (susceptible and resistant lines from Cheviot and Herdwick breeds, now at NeuroPathogenesis Unit, IAH, AFRC/MRC, Edinburgh; and from a resistant Swaledale flock now at the MAF Experimental Husbandry Farm, Redesdale, Northumberland). Most isolates of the scrapie agent, but not all, produce a faster disease in flocks with the SipA allele of the scrapie Incubation Period (Sip) gene. A goat homolog of the Sip probably exists, but this has to be proved. A murine equivalent of the Sip gene has been identified in inbred strains of mice. As in sheep, it co-localises with the PrP gene and might be identical, but this is controversial.

Various mutations in the sheep PrP gene, as evidenced by means of various molecular biology techniques (RFLP, PCR, DGGE), have been associated with the susceptibility to experimentally induced disease (i.e. the Sip alleles), or with the onset of the disease in naturally occurring scrapie (Hunter 1992; Laplanche et al. 1993). Some of them seem to be also present in other species affected by similar encephalopathy, particularly in CJD-affected humans, but a number of other mutations in the PrP gene have been associated with prion disease (Watanabe and Duchen 1993).

Because of the opposite effects of some isolates of the scrapie agent in usually susceptible and resistant lines of sheep (or mice), a marker-assisted selection for susceptibility to scrapie in sheep would probably not ensure an eradication of the disease. However, studies both on DNA polymorphism associated with the occurrence of the disease, and on the diversity of scrapie
isolates, might be useful to determine strategies for an efficient prophylaxis. Another very helpful area of research would be on the mechanisms of the vertical transmission of the scrapie agent.

Conclusions: the Main Topics Developed in Europe

Genetic maps of small ruminants, in addition to those for cattle and pigs, are being developed in Europe. Scrapie and salmonellosis-susceptibility genes have now been identified on the ovine genome; and other major genes of resistance to diseases, or involved in other physiological process, may contribute to the development of regional mapping. The primary purpose of such a map is probably to clone a major gene by accumulating markers in its vicinity until one might be sufficiently close to begin the sequencing process. Such a reverse genetic approach (from the phenotype to the gene, which then allows the identification of the relevant protein) is now classical for the identification of genetic deficiencies in humans. This approach has been used in mice for the identification of a candidate gene for mouse genes *Ity/Bcg/Lsh* by the group of P. Gros (Vidal et al. 1993). By allowing the identification of the genomic regions of interest, comparative mapping will probably remain the only possible approach when one ignores the immune mechanisms and/or the protein concerned with the observed phenotype. Furthermore, this approach provides potential genetic markers that could be useful for the identification of resistant or susceptible individuals when performing a familial analysis of any physiological trait, e.g. resistance to infection.

Comparison of the susceptibility of various animal populations (inbred or outbred lines, selected lines, flocks, breeds) is a powerful means of identification of mechanisms of resistance to natural and, more efficiently, experimental infectious or parasitic diseases. This is generally well known in laboratory animals, but multiple examples do exist in farm animals and are described in detail in this volume. Analysing differences between groups of well-identified animals will be conducted to find both new mechanisms and new genes concerned with the regulation of the immune response to pathogens. Moreover, a reasonable hypothesis is that a number of the genetic polymorphisms that are associated with known immune response genes (e.g. immunoglobulin, complement, cytokine genes) are also probably responsible for variations in the efficiency of the response to naturally occurring diseases.

In France, sheep breeding flocks contribute animals to an Individual Control Centre where a number of traits are assessed in a common environment. These traits include a parasitological test and may include other disease traits. It is necessary to have more information on the genetic
correlations between resistance to different diseases and between resistance and performance traits.

A good definition of practical selection objectives for resistance to parasitic and infectious diseases is not available. Which of the following outcomes is desirable?

• animals resistant to the establishment of the pathogenic agent?
• resilient animals supporting the presence of the agent?
• low-contaminant animals, which will diminish the general level of infection of the group?

The process of selection could depend on the genetic parameters characterising transmission of susceptibility but could also depend on the pathogenic agent. As an example, selecting animals resistant to scrapie could be dangerous in absence of detection. Animals with this genotype could be infected and, in the absence of a method to detect the agent, contaminate the environment during the incubation period before the first clinical signs appear.

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References


Breeding for Resistance to Infectious Diseases in Small Ruminants


Breeding for Resistance to Infectious Diseases in Small Ruminants


Genetics of Disease Resistance in Small Ruminants in Africa

R.L. Baker

Abstract

Disease is one of the most important biological constraints to small ruminant production in the many different agroclimatic zones of Africa. Loss of production, high levels of mortality and the cost of drugs are some of the major concerns. Current control strategies include vaccination, medication, isolation of animals from pathogens and improved sanitation for management systems. In Africa, many control strategies are limited by lack of efficient veterinary services, unavailability or high costs of drugs and vaccines, increasing occurrence of drug resistance by pathogens and limited scope to improve management cost-effectively. An attractive alternative solution is to breed for disease resistance.

There is a large and diverse range of indigenous breeds of sheep and goats in Africa, some of which appear to be genetically resistant or tolerant to disease. The limited data on between- and within-breed genetic variation in resistance to helminthiasis and trypanosomiasis are reviewed and the need for further characterisation is identified. Evidence for the genetic basis of disease resistance in sheep in countries outside Africa, suggests that breeding for disease resistance could be a viable control method. More information on genetic parameters of disease resistance and better assessment of the economic impact of disease is required to develop appropriate breeding strategies.

In Africa, diseases are a substantial constraint on sheep and goat production. They are often a major contributor, along with poor nutrition and poor management, to high annual mortality rates that can range from 30 to 50% in young stock and 10 to 30% in mature animals.

One option for overcoming the impact of infectious disease in small ruminants is the identification and use of disease resistant animals or breeds. This could proceed at the same time as other essential studies on the epidemiology and the costs of disease, development of new vaccines, chemotherapeutic drugs, health management strategies and improvement of animal health delivery systems. This paper will document the evidence in Africa for genetic resistance to diseases in small ruminants and outline some options for breeding for disease resistance.
Breeding for Resistance to Infectious Diseases in Small Ruminants

Why Breed for Disease Resistance?

Conventional approaches to disease control include vaccination, medication, isolation of animals from pathogens, improved sanitation and eradication. Lack of effectiveness of some vaccines and development of resistance of pathogens to drugs and chemicals are becoming increasingly common (e.g. Nicholas 1987; Waller 1991). In Africa, resistance of ticks to acaricides and resistance of trypanosomes to trypanocides is well documented (Young et al. 1988; Peregrine 1994). Similarly, anthelmintic resistance has been reported worldwide across the range of helminth parasites of most domestic livestock (Waller 1991), particularly in gastrointestinal nematode parasites in sheep and goats. Although a reliable assessment of the prevalence of anthelmintic resistance in sub-Saharan Africa is not available, prevalence is believed to be low or non-existent in many cases simply because anthelmintics are used rarely or not at all (Nansen 1991). However, the climate of many tropical and sub-tropical regions of Africa is highly favourable to the development of anthelmintic resistance. Thus, as anthelmintic usage increases, resistance may also increase and this view is supported by recent reports of anthelmintic resistance and multiple anthelmintic resistance in Tanzania (Bjorn et al. 1991), Kenya (Waruiru et al. 1991; Maingi 1991; Mwamachi et al. 1993) and Nigeria (Mbah et al. 1992). In Africa, the development of anthelmintic resistance and drug resistance in general, is further compounded by the use of drug preparations of questionable efficacy.

Resistance to drugs and demand for lower levels of chemical residues in livestock products and in the environment, has stimulated interest in disease control methods which are less reliant on chemotherapy. In Africa the high cost and poor availability of chemicals are further limitations on their use. Thus, there is considerable incentive to use breeds or genotypes that are resistant or tolerant to disease and do not require expensive chemotherapy.

Economic Impact of Disease

Vaccines are available for a few of the many infectious diseases of small ruminants in Africa, for example against peste de petits ruminants. Where comprehensive control campaigns have been mounted, disease prevalence has been markedly reduced. The effects of some acute bacterial and viral diseases are often temporary, and if the animal survives, recovery is usually rapid. In contrast, diseases such as helminthiasis and trypanosomiasis have chronic effects (FAO 1991, 1992). Estimates of the economic impact of the total array of diseases affecting small ruminants in Africa are not available and are difficult to obtain (Ademosun 1988).
Helminthiasis

Given that some important viral diseases can be adequately controlled by vaccination, internal parasitism by nematodes and trematodes is considered to be the most important constraint to sheep and goat production in Africa (Mack 1982; Smith 1988). Information on direct and indirect losses caused by helminth infection is limited. There are few published estimates but they suggest that production losses are generally high. Graber (1965) calculated an annual loss of 11.3% of the total economic value of sheep and goats in Chad due to gastrointestinal nematodes. Schillhorn van Veen (1973) estimated an 11% annual loss of value to that country’s sheep and goat industry from helminthiasis in Nigeria. Akerejola et al. (1979) estimated an annual loss of over US$40 million due to gastrointestinal nematodes in the Kano area of northern Nigeria, and annual mortality rates of 60% in lambs and 30% in ewes have been reported (Eysker and Ogunsasi 1980). In Kenya, haemonchosis alone has been estimated to cause an annual loss of US$25 million in sheep and goat production (Preston and Allonby 1979). In Zaire, Brito (1947) estimated an annual mortality rate of 54% due to gastrointestinal helminths alone and an additional 12% due to the combined effects of helminth and coccidial infections.

Ticks and tick-borne diseases

Tick-borne diseases of sheep and goats in Africa include babesiosis, theileriosis, anaplasmosis and cowdriosis. In many areas ticks can be a problem and frequent dipping with acaricides is carried out. Heartwater (Cowdria ruminantium infection) is an important disease of both cattle and small ruminants in Africa. It is transmitted by several species of the tick Amblyomma of which A. variegatum is the most common and can cause high rates of mortality in sheep and goats (Uilenberg 1976, 1983; Arnold and Thavassos Santos Dias 1983; Norval et al. 1992a; Camus and Barre 1988). Smith (1988) suggested, however, that tick-borne diseases do not usually cause serious morbidity and mortality of small ruminants.

A number of Theileria species occur in sheep and goats in North Africa and some of these are highly pathogenic (Dolan 1989). Integrated control strategies being developed to control T. parva include tick control, acaricides, resistant genotypes and immunisation (Norval et al. 1992b).

Trypanosomiasis

Most of the studies of animal African trypanosomiasis have been carried out in cattle. Trypanosomiasis has not been regarded as an important disease of small ruminants and the prevalence of trypanosomiasis appears to be lower in...
Breeding for Resistance to Infectious Diseases in Small Ruminants

sheep than cattle (Coulibaly et al. 1988; ILCA 1986). Kramer (1966) reported that trypanosomiasis in Nigeria was of little significance in sheep and goats and Finelle (1974) stated that sheep were seldom infected with trypanosomes under natural conditions. However, a more recent survey in tsetse-infected regions in Zaire indicates that trypanosomiasis may be more important in small ruminants than was previously thought (Makumyaviri et al. 1989). Trypanosome infections in small ruminants in East Africa (Zwart et al. 1973; Griffin and Allonby 1979a; Hendy 1988) have been associated with severe economic losses (Griffin and Allonby 1979a; Kanyari et al. 1983). It has also been suggested that small ruminants may be important reservoirs of infection for other livestock (Mahmoud and Elmalik 1977).

Genetic Variation in Disease Resistance

This review will concentrate on the larger body of evidence which is available for genetic variation in small ruminants for resistance or tolerance to helminthiasis and trypanosomiasis. Other diseases for which there is little evidence of genetic variation are discussed elsewhere in this volume.

Breed differences

*Helminthiasis.* Nearly all the studies reviewed by Gray (1991) and Baker et al. (1992) are characterised by poor experimental design, both in terms of the numbers of animals of each breed tested, and lack of information on how the breeds were sampled. In addition, very few of the studies took account of variation among sires within breeds. The magnitude of the between-sire differences can be of the same order as the largest of the between-breed differences (Gray, et al. 1987). Many of the breed differences reported could just reflect a single sire effect and hence should be interpreted cautiously.

Some breeds of sheep have been identified as resistant in a number of independent studies. These breeds include the Florida Native and St. Croix in the USA (Courtney et al. 1984; Courtney et al. 1985a, b; Knight et al. 1973; Gamble and Zajac 1992) and Red Maasai of East Africa (Preston and Allonby 1978, 1979; Bain et al. 1993; Baker et al. 1993). It is noteworthy that the St. Croix sheep originated in West Africa and are probably related to the Djallonke sheep (Bradford and Fitzhugh 1983), which are believed to be relatively resistant to endoparasites (Osinowo and Abubakar 1988; Smith 1988). Most of the breeds identified as being relatively resistant are native or 'unimproved' breeds. This presumably reflects the fact that these breeds have been under natural selection with little or no treatment with anthelmintics.
Evidence for genetic variation for resistance to endoparasites among goat breeds is limited (Preston and Allonby 1978; Cabaret and Anjorand 1984; Shavulimo et al. 1988; Richard et al. 1990; Rohrer et al. 1991). It is usually the indigenous goat breeds (e.g. the Small East African) that are more resistant than the imported exotic breeds.

Virtually all research on genetic variation to endoparasites in small ruminants has concentrated on nematode parasites. In many areas of Africa and the developing world liver fluke (trematode) infections (*Fasciola hepatica* and *F. gigantica*) are also an important constraint to small ruminant production (FAO 1992). Although it is well documented that sheep can mount an effective immune response (self-cure) to nematode parasites, it has been amply demonstrated that sheep are unable to acquire resistance to liver flukes (e.g. Boyce et al. 1987). This possibly explains why very little research has been undertaken on genetic resistance to liver fluke infections and only two studies have been published. Boyce et al. (1987) found significant breed differences in faecal egg counts and fluke counts following experimental infection of five breeds of sheep with *F. hepatica*. Barbados Blackbelly sheep were the most susceptible to infection while St. Croix and Florida Native sheep were the most resistant. Although none of the breeds demonstrated an ability to resist reinfection with *F. hepatica*, clear breed differences were detected in response to infection. In the other study Wiedosari and Copeman (1990) document relatively high resistance to *F. gigantica* in Javanese thintailed sheep, although there was no contemporaneous breed comparison.

**Trypanosomiasis.** It has been recognised since the beginning of this century that some breeds of cattle, as well as many wild animal species, possess the ability to survive and be productive in tsetse infected areas without the aid of drug treatment, where other breeds rapidly succumb to the disease (Dolan 1987; Murray et al. 1991; Paling and Dwinger 1993). This trait has been termed trypanotolerance.

There has been a considerable research effort on trypanotolerance in cattle but much less is known about trypanotolerance in sheep or goat breeds. The Dallkonke sheep and West African Dwarf goats, which are indigenous to the tsetse-infested areas of West and Central Africa and survive without the aid of chemotherapy, have been described as trypanotolerant (ILCA 1979; Toure et al. 1983; Mawuena 1987; Adah et al. 1993; ITC 1992). Studies in East Africa have also shown that the indigenous sheep (Red Maasai and Blackhead Persian) and goats (Small East Africa and Galla) are more resistant to trypanosomiasis than exotic breeds (Griffin and Allonby 1979 a, b; Kanyari et al. 1983; Munyua 1985). Whitelaw et al. (1985) failed to demonstrate any significant differences in resistance of the Small East African, Galla and their
Breeding for Resistance to Infectious Diseases in Small Ruminants

crosses with Nubian or Toggenburg goats in Kenya, following challenge with *Trypanosoma congolense*. They attributed this finding to the high virulence of the strain used. Similarly, McGuire et al. (1985) found no significant differences in resistance to trypanosomiasis among four exotic breeds of dairy goats (i.e. Toggenburg, Nubian, Alpine and Saanen). On the other hand, significant differences in trypanotolerance have been reported among strains of East African goats with those sampled from tsetse-endemic areas being more resistant than those from tsetse-free areas (Mutayoba et al. 1989).

Although the prevalence of trypanosomiasis is often higher in cattle than sheep or goats raised in the same environment (e.g. Coulibaly et al. 1988), this does not necessarily indicate that small ruminants are more resistant to trypanosomiasis than cattle. It may just indicate that small ruminants do not graze in heavily tsetse-infested areas or that the tsetse fly finds cattle more attractive than small ruminants. More research on the epidemiology of trypanosome infections in small ruminants is required to resolve these questions.

**Within-breed genetic variation**

Estimates of heritabilities and repeatabilities of resistance to endoparasites in sheep and goats in Africa are limited but those available were reviewed by Baker et al. (1992). The few heritability estimates range from 0.11 to 0.42 for faecal egg count (FEC) and haematocrit (PCV) (Rohrer et al. 1991; Baker et al. 1993), essentially similar to those found in Australia and New Zealand. Other repeatability estimates available range from 0.05 to 0.42. In some studies the low repeatability estimates for FEC were caused by the egg counting procedure. The improved modified McMaster egg counting technique (MAFF 1977) is recommended and usually gives higher repeatability estimates. It is important that the egg counting technique is standardised in any experimental study on resistance to endoparasites and that the procedure used is clearly documented.

In Africa, there is evidence that resistance to endoparasites (assessed in terms of FEC or PCV) is favourably associated with production, particularly in terms of reproduction and mortality (Baker et al. 1993). If this is found to be true generally then FEC and PCV are likely to be easier and more practical parameters to measure than resilience traits.

*Trypanosomiasis*. No estimates of within-breed genetic variation for trypanotolerance in sheep and goats have been reported, but the progress made in cattle is reviewed here since it seems likely that similar criteria will also be relevant to small ruminants. For example, the course of *T. congolense* infection
and pathophysiology in sheep has been shown to be broadly similar to that observed in cattle (Katunguka-Rwakishaya et al. 1992).

Anaemia can be assessed relatively easily in terms of PCV in infected animals and moderate to high heritabilities (0.35–0.64) have been reported (Murray et al. 1990; Trail et al. 1991 a,b,c; Trail and d’Ieteren 1992; Dolan 1993). Positive phenotypic and genetic correlations between control of anaemia and production traits (i.e. growth, calving interval and cow productivity) have been reported (Trail et al. 1991b), although the genetic correlation estimates have high standard errors and are biased—as discussed in the next section—because production was measured under parasite challenge.

The degree of parasitaemia is not as easily or reliably assessed as PCV, and the most common method used to date is the detection of trypanosomes in blood smears using the dark ground/phase contrast buffy coat microscopic method (Murray et al. 1977; Paris et al. 1982). This technique is highly specific but not very sensitive, thus resulting in low repeatabilities. For example, in Orma Boran cows in Kenya, repeatabilities of number of times cows were classed as parasitaemic within a lactation (parasitaemia recorded at 2-week intervals) were 0.07±0.07 for *T. vivax* infections and 0.24±0.06 for *T. congolense* infections (Dolan 1993).

Recently, antigen-detection enzyme immunoassays (antigen-ELISA) have been developed for the diagnosis of *T. vivax*, *T. congolense* and *T. brucei* infections (Nantulya and Lindquist 1989; Nantulya 1990). These assays are based on monoclonal antibodies that recognise trypanosome antigens specific for the three trypanosome species. The antigen-ELISA has been shown to be four times more sensitive than the buffy coat technique in monitoring *T. congolense* infections in cattle (Masake and Nantulya 1991). Nantulya (1993) has reported the development of a latex agglutination antigen test for diagnosis of African trypanosomiasis: the presence of specific antigens for different trypanosome genera in the specimen leads to the agglutination of the sensitised latex particles. The results are read within 5 minutes and virtually no equipment is required as the tests can be carried out using heparinised whole blood, plasma, or serum. If field validations demonstrate that this test has a high degree of sensitivity and specificity then it could be a very useful and simple tool for large-scale breeding programs.

Trail et al. (1992a) used the antigen-ELISA for additional assessment of trypanotolerance in N’Dama cattle in Gabon. The antigen test detected trypanosome antigen in 90% of the animals parasitologically positive. More importantly, 40% of the animals that had not been found to be positive using the buffy coat test, were shown to be positive by the antigen-ELISA test. Data from 79 progeny of 21 sires was then analysed for genetic variation in
Breeding for Resistance to Infectious Diseases in Small Ruminants

parasitaemia. The approach taken was to consider animals with positive antigen test results, but not positive buffy coat test results to have some ability to limit parasite growth. This parasite control measure had a heritability estimate of 1.08±0.50 and clearly warrants further investigation in larger data sets.

The trials with N'Dama cattle in Gabon using the antigen-ELISA also showed marked differences in the effects of *T. congolense* and *T. vivax* on animal performance. While *T. congolense* infections had significant deleterious effects on animal growth the *T. vivax* infections did not (Trail et al. 1992b). In mixed infections, which are detected more frequently with the antigen-ELISA than the buffy coat test, the significant negative regression of weight gain on the number of *T. congolense* infections was obscured when *T. vivax* data were not deleted. This result illustrates the necessity for accurate trypanosome species identification if infection effects and linkages with other criteria of trypanotolerance (e.g. PCV) are to be clarified and adequately quantified.

Further studies with N'Dama cattle in Zaire (ILCA 1992) and with Orma Boran cattle in Kenya (Dolan 1993) have shown differences in the kinetics of *T. vivax* and *T. congolense* infections, in both cases using the buffy coat test to detect parasitaemia. In both studies it was shown that infection rates with both *T. vivax* and *T. congolense* were lower in calves than their dams. This change in the proportion of *T. vivax* and *T. congolense* infections with age appears to be a common feature in the studies in Gabon and Zaire with N'Dama cattle and with Orma Boran cattle in Kenya. In calves the majority of infections were caused by *T. vivax* (or in Zaire equal proportions of *T. vivax* and *T. congolense*), while *T. congolense* was the predominant trypanosome in cows. These results suggest the ability to acquire some degree of resistance to *T. vivax* infections, and this ability may be more marked in the more trypanotolerant N'Dama cattle.

The new trypanosome antigen-detection techniques, combined with the more traditional microscopic diagnostic techniques offer possibilities for further refining reliable indicators of trypanotolerance. Further recent analyses of N'Dama cattle in Zaire indicate that changes in trypanosome species, length of time parasitaemic, intensity of parasitaemia and average PCV each have approximately equal phenotypic effects on daily liveweight gain (ILCA 1992). What is now required, to evaluate fully the usefulness of each of these traits as selection criteria, are estimates of the heritabilities and phenotypic standard deviations for each of them, the genetic correlations among them and genetic correlations of each selection criterion with production traits.
Genetic resistance to different diseases
The question of whether a breed or population of livestock resistant or tolerant to one disease also shows any resistance or tolerance to other diseases is particularly important in Africa where there is a large range of diseases that constrain production. It has been reported that trypanotolerant N'Dama cattle carry significantly lower tick burdens than Zebu or N'Dama × Zebu crossbred cattle and that N'Dama cattle may possess a degree of tolerance to some tick-associated pathogenic organisms (Mattioli et al. 1993). However, preliminary evidence suggests that N'dama and Boran cattle are equally susceptible to East Coast fever (Dolan et al. 1992).

Combined selection for disease resistance and production traits
In small ruminants in Africa, a critical question will be: what are the genetic correlations between disease resistance and production traits? From between-breed comparisons it is often assumed these may be unfavourable. For example, many of the sheep breeds with high levels of resistance to endoparasites (e.g. Red Maasai, Florida Native, St Croix) are those reputed to have low productivity in terms of reproduction, mortality and growth. However, this negative association between productivity and endoparasite resistance is not supported by within-breed genetic correlation estimates. In addition, these indigenous, ‘unimproved’ breeds are usually being evaluated in very unfavourable environments. When ‘improved breeds’ have been evaluated in these environments they have often been shown to be completely unadapted to diseases, with resulting high mortality rates.

Breeding Programs for Disease Resistance
There is a wide variety of small ruminant production systems in Africa, ranging from intensive systems where land size and flocks are very small, to extensive rangelands where larger flocks are run at low stocking rates (Wilson 1982). In these situations, small ruminants are not only kept for meat, milk, fibre and skins, but also contribute manure for crop production. They are also a source of capital investment, are an important way of storing wealth and can play important social and cultural roles. Defining breeding objectives in such systems is likely to be extremely difficult (e.g. Hetzel and Seifert 1986) because of unknown elements such as the relative magnitude of costs and returns, and important socioeconomic factors which can often be of overriding significance (Anteneh 1982). For example, many livestock owners in Africa keep large numbers of animals as a form of risk avoidance with little concern for the efficiency of meat or milk production. Thus the
Breeding for Resistance to Infectious Diseases in Small Ruminants

important traits to include in the breeding objective of African production systems may be very different from those in other production systems which seek to improve efficiency and profitability. This is well illustrated by an analysis of economic returns from small ruminant production in South West Nigeria (Upton 1985). In this production system, decreasing mortality and increasing reproduction brought the highest economic returns, while increasing growth rate was of little economic significance.

In Africa one of the first questions is how to utilise breed variation most efficiently. Most breed evaluations carried out to date have compared only purebred populations (e.g. Baker et al. 1992). Although this will provide estimates of additive genetic variation among breeds it does not provide estimates of heterosis and/or epistatic effects which are required to formulate optimum crossbreeding strategies (Dickerson 1969). If, however, some indigenous African breeds are found to be relatively resistant to diseases then one option will be to carry out multi-trait genetic improvement programs within that breed or population. If crossbreeding strategies are indicated (e.g. because the performance levels of the resistant breed are low), then the ranking of resistance in purebred performance is useful in predicting average transmitted effects in crosses (ILCA 1991, 1992). However, the correlation between purebred and crossbred performance is limited by breed differences in level of inbreeding, in epistatic interaction and by sampling errors of estimation of breed means. If crossbreeding strategies are to be employed then it will be important to estimate the appropriate parameters. The possibility of heterosis for disease resistance should not be ignored (Zijpp et al. 1990).

With the evidence that genetic variation in resistance to nematode infections within breeds can be as great as that between breeds, both in sheep (Barger 1989) and cattle (Kaufmann et al. 1990), Pfister (1991) suggested that breeding programs in developing countries should concentrate on genetic improvement of local indigenous breeds. This suggestion is logical but it is important to emphasise that genetic variation among indigenous sheep or goat breeds in Africa is likely to be larger than that found among breeds of sheep in Australasia. Further, there is very limited evidence on the amount of genetic variation within indigenous African sheep and goat breeds for resistance to endoparasites (Baker et al. 1992). It is therefore likely that breeding programs in Africa will utilise both between-breed and within-breed genetic variation for disease resistance.

Pfister (1991) posed a number of questions which need to be answered before breeding programs for resistance to endoparasites in Africa can be implemented successfully. These include socioeconomic issues, profitability
and the acceptability of programs by local livestock owners. The breeding program proposed by Pfister did not envisage stopping the use of anthelmintics, but the development of genetically resistant animals which would receive fewer anthelmintic treatments. Pfister's proposal was for on-farm recording and evaluation but his scheme could be increased in scope to include aspects of a group breeding system, including a nucleus flock or herd as suggested by Cummins et al. (1991).

Genetic Markers and Marker-assisted Selection

Recent advances in molecular biology to identify polymorphic genetic markers may be used to improve rates of genetic progress through marker-assisted selection (e.g. Soller 1978; Lande and Thompson 1990; Meuwissen and van Arendonk 1992; Brascamp et al. 1993, Nicholas, this volume). In theory, there is no reason why this technology should not be used in Africa (Teale 1993). For example, there is a major research program at the International Laboratory for Research on Animal Diseases in Nairobi, Kenya, to identify genetic markers for trypanotolerance in families generated by crossing N'Dama and Boran cattle (Teale 1991, 1993).

Use of genetic markers in animal breeding involves a number of important activities as follows:

- Generation of polymorphic DNA markers.
- Establishment of a linkage map of the markers.
- Designing and generating resource families which are segregating for the loci of interest (Quantitative Trait Loci—QTL) and the markers. These can be F₂ families, backcross families or large families from heterozygous F₁ sires.
- Ensuring that the phenotype for the QTLs can be accurately assessed.
- Detection of linkage and estimation of the recombination fraction between markers and QTLs.
- Use of marker-QTL linkage associations in breeding programs (i.e. Marker-assisted Selection-MAS).

A linkage map with sufficient resolution to begin screening the bovine genome for genes (QTLs) which control biologically and economically important characteristics of cattle is now complete (Barendse et al. 1994). It is likely that similar maps will soon become available for small ruminants and there is a need to develop facilities in Africa for the detection of QTLs for disease resistance.
Concluding Comments

Over 95% of Africa's ruminants are of indigenous breeds which provide smallholder rural farmers with protein, income and a secure form of investment (Rege and Baker 1993). Small ruminant breeds have evolved over centuries in diverse African environments and are likely to be adapted to high levels of disease challenge. Disease resistance and other adaptive traits such as heat tolerance, ability to use poor quality feeds and to survive with sporadic supplies of feed and water have enabled small ruminant production in vast areas of the continent where crop production is impractical. They are also an important component of crop–livestock production systems.

Accelerating demands of a growing human population and pressures of economic development are threatening the security and survival of many indigenous African breeds which, until now, have been a stable part of their particular ecosystems for hundreds of years. These breeds are threatened because of an increasing tendency to introduce exotic breeds, to rely on a narrow range of supposedly more profitable breeds and to interbreed among indigenous breeds.

It is essential that this unique genetic diversity is thoroughly characterised and that conservation strategies are implemented (Rege and Baker 1993). Development and utilisation of indigenous breeds may benefit not only Africa, but some of their unique characteristics, such as genetic resistance to disease, could have an important impact on livestock production throughout the world.

References


Breeding for Resistance to Infectious Diseases in Small Ruminants


132


Breeding for Resistance to Infectious Diseases in Small Ruminants


Breeding for Resistance to Infectious Diseases in Small Ruminants


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