Cattle Breeding for Disease Resistance

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Effective production of animals for meat, milk and fibre is often disrupted by diseases causing considerable monetary losses. Selection pressure on commercially important traits under stressful production setting may increase incidence of disease, eg. Mastitis is more common in high yielding milch cows than in low yields. The spread of diseases among domestic animals are traditionally limited by eradication of infe cted stock, isolation of principles of hygiene or vaccinations and treatment of affected stock. Many diseases how ever cannot be controlled by these means and increasing use of drugs has to be resorted to eliminate such pathogens or their vectors. Regular use of therapeutic agents minimizes the selective advantage of natural resistance in the animal population further more pathogens are encouraged to diversity into forms that are resistant to many drugs. Moreover excessive use of antibiotics and pesticides could have serious adverse effects on environment.

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The prevalence of certain diseases was found to be strictly under genetic control whereas certain others were caused due to a combination of genetic pre disposition and exposure to pathogens. Genetic control of diseases, if any may be the result of presence or absence of specific receptors that are inherited. eg. Resistance to infection by K-88 strain of *Escherichia coli* is recessive and would have been eliminated from animal population by selective breeding but susceptible animals remain in the population because the maternal antibodies allow some protection.

Genetic strategies for disease resistance

(1) Direct selection for disease resistance

In cases where the resistance to a particular disease is moderately to highly heritable, direct selection among the breeding stock for this desirable trait could bring about improvement. Mainly four approaches are used under direct selection.

(i) Observation of the breeding stock under normal production conditions: This is the simplest method but would not be informative without incidence of the disease. For example, African cattle breeds like N'dama are resistant to Trypanosomes under natural environment unlike Europian *Bos taurus*.

(ii) Challenging the breeding stock: This approach if effective but might prove to be disastrous and costly depending on the severity of challenge, hence not advisable if death occurs due to the disease. Moreover there is negative effect on the production of breeders.

(iii) Challenging sibs or progeny of breeding stock: This method is an improvement of the previous approach. The overall production of the herd is affected adversely and accuracy will be limited if sufficient number of progeny or sibs is not tested.

(iv) Challenging clones: By raising a large number of clones of embryos from planned mating of breeding stock will provide sufficient number for accurate evaluation and selection. When one set of these clones are challenged with specific diseases, selection based on the results could be practiced on an identical set of clones. Since the animals tested are clones, accuracy would be equal to test the individuals themselves.

Problems involved with direct disease challenge and

selection includes standardization of the level of challenge exposure to a particular disease and maintenance of isolation facilities for this type of selection. Selection difficulties would arise if there were antagonistic correlations between disease resistance and production traits. An index approach based on weightage of different factors contributing to a trait would be useful. This will require accurate estimates of all the genetic correlations between disease resistance and performance traits.

(2) Indirect selection for disease resistance

Due to difficulties in selecting for disease resistance under challenging environment indirect selection by selecting other correlated characters have been proposed.

(i) Selection for antibody response: In cases where candidate gene information is not readily available the approach of selections for the trait of immunocompetance can be employed to enhance disease resistance (Rothschild, 1989). Early studies with mice (Biozzi *et al.*, 1980) have revealed that genetic control of antibody response to sheep RBC was moderately heritable and that selection for humoral immune response to other antigens. In cattle and sheep, experiments have revealed genetic variation for immune response to variety of antigens including chicken RBC, human serum albumin and infectious bovine rhinotracheits. These results suggest a genetic control of immune response exists in most livestock species.

(ii) Selection based on in vitro tests:Invitro methods include phagocytic and bactericidal action of peripheral blood monocytes against disease agents such as *Salmonella typhimurium* and *Straphylococcus aureus* (Lacey *et al.*, 1990). Other methods include neutrophil metabolism and phagocytic activity and lymphocyte blastogenesis in response to antigens. The fact that *in vitro* procedures and their relationship to actual diseases resistance is unknown doubts its efficiency as a basis for selection.

(iii) Marker Assisted Selection (MAS): Marker assisted selection by tagging of economic trait loci (ETL) genes with a biochemical or genetic marker permits rapid genetic gain in specific traits. eg. In cattle, Bovine cardiomyopathy, a genetic disease was linked to 'B' blood group system or Weaver disease in Brown swiss was associated with increased milk production and can be identified by microsatellite (genetic) marker, TGLA116. This approach requires the establishment of diverse markers in the cattle genome that can be correlated to economic traits like resistance to specific diseases using appropriate statistical techniques.

a. Major histocompatibility complex (MHC) locus

MHC genes are intimately associated with both disease resistance and immune responsiveness. All higher life forms are known to possess MHC that codes for predominant cell surface proteins of each species. These antigens are markers of "self" and are unique for animals other than identical twins or clones. MHC encodes for three classes of proteins – Class I, Class II and Class III of which Class I proteins are highly polymorphic and Class II antigens are less so while Class III molecules show limited polymorphism. The Class I antigens act as restricting elements in T cell recognition of virally infected target cells and are necessary to generate an immune response. The class II genes control the interaction of T cells, B cells and macrophages in the generation of the humoral immune response and participate in aspects of cellular immunity. The Class III genes are intimately involved with the compliment cascade, which ends with the lysis of the cell or virus to which antibody has bound.

In cattle the BoLA (Bovine MHC) complex activity has been associated with intestinal parasites, tick susceptibility, and mastitis (Spooner *et al.*, 1998). There was a clear association of BoLA haplotypes with progression of subclinical bovine leukaemia virus infection at both family and herd level (Lewin *et al.*, 1988).

Trail *et al.* (1989) found an association between a serologically defined class I phenotype and susceptibility to the effects of trypanosome infection in N'Dama cattle. Weak associations of individual class I MHC antigens with high or low levels of infestation with *Boophilus microplus* and with low nematode faecal egg counts were described by Stear *et al.* (1990).

b. Nramp 1 gene (Synonyms: Bcg/Lsh/Ity)

Nramp I gene controls the capacity of mature tissue macrophages to restrict the proliferation of ingested parasites in the reticulo endothelial organs and provides natural resistance to intracellular parasites as *Mycobacterium bovis, Leishmania donovani* and *Salmonella typhimurium* by direct action. Sequencing of

Nramp 1 revealed that it code for a macrophage – specific polytrophic protein which function by a cytocidal/cytostatic mechanism at early stage of the macrophage – parasite interaction (Vidal *et al.*, 1995). It was further shown that an amino acid substitution in the gene product would render the animal susceptible to infections.

Cases of natural disease resistance in Cattle

(i) Trypano tolerance

Pathogenic species of salivarian trypanosomes are present throughout Africa, Asia, South America and the Middle East affecting cattle, sheep, goat, buffalo, pig, horses, camel, wildlife and man. In cattle, *T. congolense, T. vivax* and *T. brucei* cause disease either individually or jointly. These trypanosomes are transmitted cyclically by tsetse flies. The present situation in which current methods of control like control of vector and treatment of affected herds and unavailability of vaccine, the eradication of this disease is not possible. There is increasing consideration for the use of trypanotolerant breeds of animals in endemic areas to counteract loss of animals and production.

(ii) Resistance to *Theileria* species

Tropical theileriosis (*Theileria annulata*) and East Coast fever (*Theileria parva*) are transmitted by ticks and kill susceptible cattle in about 20 days. Local animals were found to be more resistant to the infection than imported breeds. European cattle and their crosses exported to the tropics are susceptible. The indigenous Zebu cattle (*Bos indicus*) and the native African *Bos taurus* resistant to *T. annulata* infection.

Host susceptibility to theileriosis swamp buffalo (*Bubalus bubalis*) is noteworthy as it is highly refractory to tropical theliriosis but is highly susceptible to East Coast fever.

The potential components of resistance to these parasites includes:

(i) Resistance to ticks: Zebu cattle were observed to be more resistant to one host tick *Boophilus microplus* than exotic breeds. Resistance to ixodid ticks and particularly resistance to the two or three host vectors of bovine theileriosis like *Hyalomma* and *Rhipicephalus* had a major role to play in determining infection of cattle in endemic areas. Morphological characters such as skin thickness, number of skin folds and physiological adaptations like high heat tolerance, high sebum secretion and higher surface temperature (due greater number of arteriovenous anastomoses in animals).

(ii) Resistance to sporozoite entry into cells of immune system: These diseases involve the invasion cells of immune system by the sporozoites and transforming them to rapidly growing cells with the parasite dividing in synchrony with the host cell, producing the pathagnomonic symptoms. There could be difference in susceptibility between cells of different breeds which is reflected as resistance to the particular disease.

(iii) Ability to control pathology: Leucopenia and anaemia are the pathagnomic symptoms in theileriosis. A severe drop in the PCV of affected cattle is observed. There is high correlation between parasitaemia, the drop in haemotocrit and mortality. There is a strong genetic component in the ability of cattle to maintain their PCV at normal level under challenge.

(iv) Immune response: There is evidence that the most important protective mechanism in both diseases is a cytotoxic T cell mediated killing of parasite infected cells. Immune animals generate a MHC restricted immune response in which frequency of class I antigen varies in different groups of animals. This might be the basis of innate resistance.

Conclusion

The exploitation of natural resistance existing in the population depends on pinpointing the exact mechanism of conferring resistance. Once the specific alleles for disease resistance or specific markers linked to disease resistance are identified they can be transferred to create transgenic animals with improved disease resistance.

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