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Advances in disease control of tick and tick-borne diseases

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Abstract

In Uganda, the major tick-borne diseases of economic importance are East Coast Fever (ECF) caused by *Theileria parva*, anaplasmosis caused by *Anaplasma marginale*, babesiosis caused by *Babesia bigemina* and heartwater caused by *Cowdria ruminatium*. These diseases are transmitted by *Rhipicephalus appendiculatus, Boophilus decoloratus* and *Amblyomma variegatum*, respectively which are widespread throughout the country and lack seasonality. The control of ticks and tick-borne diseases (TBD) has been one of the most important emphases of the Veterinary Department. Until recently, control of TBDs has relied mainly on restriction of cattle movement and use of acaricides which are applied on animals in dips, or as sprays and hand dressing. However, recent years have seen very substantial improvements of methods for the control of ticks and TBDs. New drugs have been intrnduced for the treatment of TBDs. There are now highly effective drugs for treatment of theileriosis, particnlarly ECF. New generations of acaricides whieh are very efficacious are now available. Infection and treatment method of immunisation has been devised and introduced.These control methods either individually or combined have been successful in controlling ticks and TBD and has caused the general improvement in the conditions of the cattle and increased the cattle population. The tick control measures using acaricides have enabled highly productive and susceptible exotic cattle to be kept in Uganda, a task that seemed impossible 40 years ago. Immunisation against ECF together with tick control, have allowed more Ugandan farmers to raise higher prnducing exotic cattle breeds without suffering from the high costs and losses due tn ticks and TBDs.

Key words: Ticks, diseases, control, economic importance

Introduction

In Uganda, as throughout sub-Saharan Africa, urbanisation and human population growth are driving agriculture towards intensification. There is an increasing pressure to improve productivity so that the growing demand for animal products can be satisfied. Such is the case of the dairy sector which has experienced noticeable developments over the last four decades. A number of dairy production systems has evolved in the country, all of them based upon high yielding exotic breeds or their crosses.It has also been observed that the herd structure of indigenous animals in Uganda is gradually changing to crosses, due to the continuing crossing of the indigenous animals with exotic bulls (LSP/DAR report,1996). However, a number of factors limit further development of livestock industry in Uganda and these include diseases, poor management, inadequate nutrition and lack of farm inputs. One of the major health impediments to livestock improvement is attributed to ticks and the diseases they transmit (Mukhebi *et al*., 1992).

In Uganda, the major tick-borne diseases (TBDs) of economic importance are East Coast Fever (ECF) caused by *Theileria parva*, anaplasmosis caused by *Anaplasma marginale*, babesiosis caused by *Babesia bigemina* and heartwater caused by *Cowdria ruminatium*. They are transmitted by *Rhipicephalus appendiculatus*, *Boophilus decoloratus* and *Amblyomma variegatum* respectively, which are widespread throughout the country and lack seasonality.

Ticks and TBDs cause considerable economic loss to individual farmers and Government. Such losses can be classified into direct aod indirect production losses, through costs incurred in controlling the diseases, in providing research and training and in extension work on TBDs. Such losses vary widely within a country in both time and space due to differences in livestock production systems, cattle types, level of disease risk, disease control policies and programmes, cost and price structures (Mukhebi,1996). More importantly, theileriosis caused by *T. Parva*, combined with babesiosis, anaplasmosis and cowdriosis continue to restrict the introduction of improved breeds of cattle in most parts of Uganda.

The percentage of losses due to TBDs varies in different areas and breeds. It is estimated that the overall loss of the calf crop in indigenous cattle is between 10 to 30% over the greater part of the country (Okello-Onen *et al*., 1994; Otim, 1989). Production losses are attributed to debility, morbility and mortality due to ticks and TBDs. Generally, the animals which recover from TBD infections may suffer from weight loss, produce low milk yields, provide less draught power and may experience reduced fertility and delays in reaching maturity (Mukhebi and Perry, 1992).

With the introduction of high producing exotic cattle breeds, the need to reduce the negative impact of ticks and tick borne diseases dramatically increased. The affected countries including Uganda, have been searching for methods to economically control ticks and TBDs in cattle since the beginning of the century. For countries which have ECF disease, the improvement of ECF control strategies became research priorities within the Veterinary profession.

For many years and until recently the conventional methods of controlling ticks and TBDs have relied mainly on restriction of cattle movement and use of acaricides which are intensively applied on animals in dips or as sprays and hand dressing to kill the ticks. Live vaccines for anaplasmosis, babesiosis and cowdriosis have been in use for several years. Despite this, the intensive application of acaricides on cattle has been required mainly to control *R.. appendiculatus*, the principal vector of *T. Parva* for which no vaccine was available then.

However, significant research effort has resulted in very substantial improvements of methods for the control of ticks and TBDs. New drugs have been introduced for the treatment of TBDs.New generations of acaricides which are more efficacious are now available. Infection- and-treatment method of immunisation has been devised and introduced.This paper highlights tick control, chemotherapy and immunisation as control tools that have made an impact on livestock development in Uganda.

Tick control

Tick control has been used as the means of controlling the diseases caused by *T. parva* since the early part of the century, when Lounsbury (1904) discovered that ECF was transmitted by the tick *R.. appendiculatus.*

Prior to the introduction of chemical compounds for tick control, certain cultural practices such as hand picking of ticks, burning of grass and use of some hedge plants as repellants were widely used by cattle keepers. Although these practices had limited impact on ticks, they were part and parcel of animal husbandry practices then. However, the introduction of acaricides in 1930s made tick control easier and subsequently caused most of the cultural practices to be abandoned (Okello-Onen *et al.*, 1992).

It has been reported that animals were dipped to control ticks as early as 1935 (Kudamba, 1991; Okello-Onen *et al.*, 1992). However, modern tick control gained momentum only after the second world war. In 1947, dipping trials using BHC and DDT were conducted by the central laboratory at Entebbe.The major trials took place in Ngogwe, Kyaggwe. Results for the first few months was spectacular, but later, the tickicidal power of these compounds deteriorated and the trials were discontinued.

In 1949, over 2000 cattle in Ankole, were experimentally sprayed weekly with gammatox resulting in an 85% reduction in ticks in months and marked cattle improvement. By 1952 Ankole had 40 cooperative centres for spraying cattle. In 1950, Toxaphene was tested and found to be more effective than BHC and DDT. By 1957 approximately 250,000 cattle were being sprayed regularly and the figure rose to 300,000 in 1958.

In 1964, there were 544 spraying centres for cattle in Buganda and Ankole, while Lango, West Nile, Busoga and Bukedi showed increased interest. In addition, 12,545 gallons of pesticide was sold compared to 9,547 gallons in 1963. Furthermore, it was in 1964 that the Government of Uganda launched the first ever large-scale compulsory tick control scheme in Kyaggwe, involving 44,000 cattle which were sprayed in 97 spraying centres. This Scheme was financed by USAID and acaricide was free. The scheme was considered successful and the indigenous cattle population increased from 44,000 (1964) to 55,000 (1966). Exotic cattle increased from 750 in 1964 to 2,300 in 1967. There was general improvement in the condition of cattle and maturation age of cattle dropped from 6 to 3.5 years.

In 1968 compulsory tick control was declared throughout the country under statutory instrument No. 101 of 4th July. Farmers were required by law to control ticks. The Uganda National Tick Programme was initiated to assist farmers to comply. By the end of 1968, 39% cattlehad been dipped/sprayed and at the end of 1970 there were 771 completed dips/spray races compared to 432 in 1969 and 50% of 4.28m cattle were being dipped/sprayed. Development of tick resistance to Toxaphene starting in 1968 led to its phasing out in 1980 and replacement by organophosphorus compounds of which, Supona and Steladone are still in use and considered effective.

Over the years new acaricides have been developed and tested for efficacy in killing ticks and have been released in the market for use by farmers.These include new generation of acaricides,the synthetic pyrethroids which includes Bayticol pour-on (1986), Décatix (1989), spot-on (1990), the amidine such as Taktic (1991) and Ectomin (1994) are all very efficacious in killing ticks.

The effectiveness of tick control is very much dependent on: The strict adherence by farmers to the recommended regimen of acaricide application and the rate of build-up of tick populations resistant to the acaricides in use.

ECF and other TBDs can be controlled effectively when acaricides are applied rigorously over a long period of time. Unfortunately, under such conditions cattle become highly susceptible to tickborne diseases so that explosive situation results when there is a breakdown in tick control (Lawrence *et al.*, 1980) and besides, this approach increases environmental pollution.

The main advantages of acaricides in controlling TBD have been simple methods for their application which facilitated their use under a range of conditions in the field. The practice of cattle dipping has been widely accepted and understood by farming communities, governments and donors, and in general, acaricide application has proved effective in the prevention of TBD transmission. The main disadvantages of acaricides have been the rate at which their costs have increased relative to the value of cattle and cattle products, the development of acaricide resistance in ticks, adverse effects of intensive tick control on endemic stability for TBDs, environmental and food contamination by acaricides and their residues and the difficulty in sustaining an infrastructure to apply them effectively on a long-term basis. Furthermore, acaricides have failed to eradicate ticks from large areas (Norval *et al.*, 1992). Tick control however, is the single most important method that has enabled introduction of and sustaining highly productive cattle, a task, that seemed impossible 40 years ago and thereby modernising livestock agriculture in Uganda.

Chemotherapy

Several groups of compounds have been used in the chemical control of babesiosis (Kuttler,1988) of these only Imidocarb dipropionate, diminazene aceturate and tetracycline antibiotics remain freely available in most endemic countries. On the other hand, tetracycline compounds have been effective in the treatment of anaplasmosis and heartwater. Because of the need for higher dosages and longer treatment regimes for anaplasmosis, the use of drugs is generally limited to control outbreaks and not to sterilise carriers. Imidocarb dipropionate (Imizol[R], Pitman Moore) is an effective treatment for both babesiosis and anaplasmosis. However, its cost relative to diminazene makes its widespread use unlikely. In addition, Imidocarb has a prophylactic effect for babesiosis for six weeks at a dose rate of 2 ml/100 kg, but it is not satisfactory for long-term use due to toxic effects with prolonged use (Jorgensen,1991).

In ECF, unlike many of the other parasitic diseases, the majority of developments in control by chemotherapy have occurred in the last twenty years. Before that time, farmers had the option of slaughtering affected cattle or hoping that they would recover. Supportive therapy using drugs such as oxytetracyclines had only a limited effect.The search for an active drug against ECF has been hindered by the lack of a laboratory model of the disease. The search for effective chemotherapeutic agents for the treatment of ECF has been in progress for over 80 years (Dolan,1981) But it was only in 1976, that McHardy and others, showed that menoctone had antitheilerial activity. Later, parvaquone, was formulated and found to be very effective for the therapy of clinical infections induced by *T. parva* Muguga (McHardy *et al.*, 1979). In Uganda, after experimental and clinical trials were carried out (O. Bwangamoi and C.P. Otim, Unpublished results, 1983), parvaquone was registered for use under the trade name Clexon[R](Wellcome).

A potent new anti-theilerial drug, buparvaquone (Butalex[R],Wellcome) was shown to suppress early developmental stages of *T. parva* (McHardy and Wekesa, 1985). In Uganda , the clinical field trials showed that Butalex[R] was effective against ECF (C.P. Otim, Unpublished, 1990). In the field, its use for the treatment of ECF has been recommended at a dose of 2.5 mg/kg.

Schein and Voigt (1981) had reported that the more soluble lactate salt of halofuginone was also effective in the therapy of both *T. parva* and *T. annulata* infections at doses of 1-2 mg/kg. It showed antischizont effects but no effect against the piroplasm stage. Extensive laboratory and field trials were carried out in Kenya and it was found to be effective (Dolan, 1986). In addition, clinical trials were undertaken in Kenya (Chema *et al.*, 1987) and in Uganda (C.P. Otim, unpublished, 1989) and halofuginone under the trade name Terit[R] (Hoechst AG) became commercially available for the treatment of theileriosis in Kenya and Uganda, respectively.

All these drugs are most efective when administered during the early stages of the disease. The results of treatment have been somewhat varied when administered at the advanced stage of the disease. Two major problems appear to be preventing the widespread adoption of chemotherapy as a control strategy. There are often difficulties in the early diagnosis of the disease when chemotherapy is most likely to be effective. The second problem is the relatively high cost of drugs in both local and foreign currency terms. Notwithstanding the foregoing problems, these drugs have played a crucial role in controlling ECF in improved cattle introduced into endemic areas prior to immunisation and when vector control schemes breakdown. They have been responsible for boosting the farmers– confidence in keeping the exotic cattle and given the veterinarian an alternative choice for controlling ECF.

Immunisation

The blood vaccines against babesiosis and anaplasmosis have been widely and successfully used in Australia, South America and South Africa and, apart from a few problems with contamination (eg. with bovine leucosis virus), have generally been reliable. A similar vaccine for the control of heartwater is widely used in S. Africa

In ECF disease, the few animals that recover spontaneously are solidly protected against homologous parasite strain for up to 31/2 yrs (Burridge *et al.*, 1972). That protection seems to be the result of cell-mediated immune mechanisms. While serum from immune animals (cattle) contains antibodies against all stages of the parasite (Burridge and Kimber, 1972), antibody is not considered to play a role in the protection seen in recovered animals. Transfer of immune serum to naive cattle fails to protect against disease (Muhammed *et al.*, 1975) and Emery (1981) demonstrated that animals immunised with heat-killed schizont -infected cells or semi-purified schizont antigens were not protected against challenge.

Methods of immunisation

Transfer of schizont-infected cells.

In 1911, Theiler showed that it was possible to protect cattle from infections with *T. parva* by inoculating animals with cells from spleen and large lymph nodes dervived from cattle that had died of ECF. This method was reinvestigated but without any improved results (Brocklesby *et al.*, 1965; Jarrett *et al.*, 1966).

Infection and treatment method of immunisation.

Neitz (1953, 1957), was the first to demonstrate that in *T. parva* infections induced by ticks, administration of tetracyclines over a prolonged period of 8-12 doses resulted in cattle becoming effectively immunised without adverse effects. Later, workers observed that oxytetracyclines when administered during the incubation period could alter the course of clinical ECF. Some of the animals thus treated did not die of the disease and were later protected from challenge (Brocklesby and Bailey, 1962). This effect was enhanced when long acting oxytetracycline was given in a single dose of 20 mg/kg at the time of infection with the sporozoite stabilate, resulting in the development of immunity to homologous *T. parva* stabilate infection with minimal clinical response (Norval *et al.*, 1992).

Cross-immunity studies and field challenge of animals immunised by the infection-and-treatment method showed that, the different immunogenic types of *T. parva* existed in the field (Young *et al.*, 1977) and these sometimes broke through the chemotherapeutic cover. This led to the search for a A master@ stock which would induce broad protection in immunised animals (Mutugi *et al.*, 1990).

In a series of experiments, a combination of three stocks (*T. parva* Muguga, *T. Parva* Kiambu 5 and buffalo-derived *T. parva* Serengeti transformed) collectively given the name AMuguga cocktail@ was shown to afford very effective protection against *T. parva* both in the laboratory and field in many parts of East and Central Africa (Musisi, 1990). In Uganda, (Mutugi and otim, 1991; Mutugi *et al.*, 1995; Moran *et al.*, 1997) have shown that Muguga cocktail vaccine effectively protects cattle against local parasite strains and have thus recommended its use on private farms. However, only partial protection is reported in cases where buffalo derived *T. parva* exist (Musisi, 1990). In addition, the vaccine utilises live potentially lethal parasites, has a storage and delivery problems and there is the risk of transmission of other pathogens. Despite these limitations, the method is the most practical one available and in those areas where there is no intrusion of buffalo, the immunised cattle are effectively protected against heterologous challenge.

Novel vaccines.

Alternative methods of immunisation against ECF and other TBDs are being sought. This has led to the identification of an antigen of relative molecular mass of 67 kDa named p67 located on the surface of sporozoites of *T. parva* (Musoke *et al.*, 1993). This antigen has since been developed into a vaccine against ECF by Scientists from ILRI and is undergoing field trials.

Although vaccines for ECF are new, the farmers and veterinarians have enthusiastically embrased them because the vaccines serve as additional control measures to the already existing methods.

Conclusion

Tick control using acaricides, chemotherapy and immunisation have had a major impact on reducing the deleterious effects of ticks and tick-borne diseases. They have enabled the otherwise susceptible and highly productive cattle to be kept profitably in Uganda. However, single methods should not be relied on to control ticks and TBDs. Integrated approaches are required, which combine an appropriate balance between tick control, vaccination, chemotherapy and management. Research into ways of achieving integrated tick and TBD control is therefore required.

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