

TRYPANOSOMOSE OF RUMINANTS



Rational use of trypanocides

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Animal trypanosomosis, transmitted by tsetse flies are a major hindrance to livestock production in sub-Saharan Africa. In infested areas they reduce the livestock production by 50% in terms of meat and milk production. Animal traction is reduced significantly by trypanosomosis and hence the total agricultural production is also reduced by 10%. It is estimated that without the presence of tsetse flies 90 million additional cattle could be produced.

To treat trypanosomosis, the most commonly used method is to apply trypanocidal drugs. The market of veterinary drugs in West Africa is estimated to be more than 14 million CFA. The proportion of trypanocidal drugs within the total of veterinary drugs varies between 20 and 50% depending on countries.

Diagnosis : an important prerequisite

Clinical diagnosis, which is generally limited to suspicion, relies on the observation of non specific signs. Trypanosomosis sometimes manifests in an acute form with a sudden rise in temperature accompanied by recumbence, lacrymation and oedema (picture 1). Most often a chronic form with signs such as undulating fever and anaemia accompanied by paleness of the mucous membrane, weakness, respiratory distress, loss of appetite and weight loss is observed. Those bouts of fever alternate with periods of apparent remission. Enlargement of the lymph nodes, watery eyes, cutaneous swellings, nervous signs, oedema and abortions are sometimes observed. In the final stage of chronic infection animals are cachectic (lose a lot of weight).

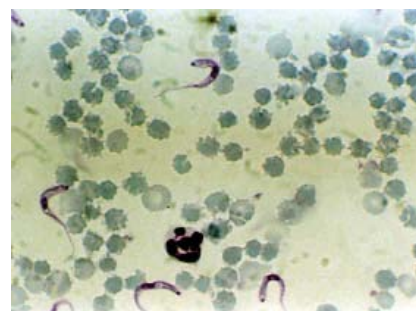


Picture 1. A recumbent animal suffering from trypanosomosis (photo M. L. Dia)

The microscopic demonstration of Giemsa-stained parasites either directly from blood or tissue fluids or after concentration of blood and fluid is a routine method of diagnosis (picture 2 and 3). Although the method allows the confirmation of the presence of trypanosomes, it is not very sensitive. In all cases information brought by herdsmen is very important in the identification of sick animals.



Picture 2. Microscopic examination of blood smears. (photo M. Desquesnes)



Picture 3. Trypanosomes in Giemsa-stained smears (photo M. Desquesnes)

Trypanocides available in West Africa

Depending on countries and the preferences of veterinarians and livestock farmers, many derivatives of urea (suramin), quinapyramine diminazene phenantridine (homidium isometamidium) and arsenic products (melarsamine) are used to treat against animal trypanosomosis. The main products available in West Africa are shown in the table 1 with the indications and dosage as well as under which brand name they are available. They may, in those commercial preparations, contain other ingredients having a minor complementary role.

Beside those products, chloride and ethidium are also used, mostly in some Anglophone East African countries as well as Mauritania and in Senegal. Ethidium products are known for their high toxicity, especially for their ability to cause inherita-

ble genetic damage. It is thus not advisable to use ethidium products in the field.

Diminazeme aceturate (Berenil®, Veriben®...) and isometamidium chloride (trypamidium®, Veridium®...) are the main trypanocide products used in ruminants in West Africa. Diminazeme aceturate is a curative drug while isometamidium chloride, which has a long action, is a preventive trypanocide.

Table 1. Main trypanocidal products available in West Africa.

Generic names	Route	Dosage rate	Indications	Animals	Trade names
Diminazene aceturate					
Solution for use : 7 % sterile water	IM	3.5mg /kg; 5ml / 100kg	Systmatic (repetitive) treatment (prophylactic)	All species of, trypanosomes; cattle, small ruminants, equine, camels. Possibly used in dogs, but with care (medical monitoring)	Berenil®, Veriben®, Trypan®, Trypadim®, Trypazene®, Trypamyl®, Diamyl® Diminazen®
		7mg/kg ; 10 ml/100 kg	or individual curative treatment		
Isometamidium chloride					
Solution for use : 1 % sterile water	IM (deeply) or strict IV	0.5-1 mg/kg; 5-10 ml/100 kg	chemoprevention	cattle, small ruminants, horses, camels, water buffaloes, dogs	Trypamidium®, Samorin®, Veridium®, Securidium®
Mel Cy					
Solution for use : 0,5 % sterile water	SC or IM	0.25 mg/kg; 5-10 ml/100 kg	<i>T. evansi</i>	camels and horses	Cymelarsan®
Suramin					
Solution for use: 10 % sterile water	IM or IV	7.5 ml/100 kg	<i>T. evansi</i>	camels, horses and dogs	Naganol®
Quinapyramine (methyl sulfate)					
Solution for use : 10 % sterile water	SC	5 mg/kg	all species of trypanosomes	cattle, small ruminants, pigs and dogs, horses and camels	Anthrycide® Trypanocide® Trybexin® Noroquin®
		5 ml/100 kg			
		3 mg/kg			
		3 ml/100 kg			
Quinapyramine sulfate and chlorure					
Solution for use : 17 % sterile water	SC	2.5 g/15 ml 5 ml/100 kg	chemoprevention	cattle and camels; should be used in horses but a risk of reaction is possible	Anthrycide® Trypacide®, Tribexin® Noroquin®
Homidium bromide		Highly toxic (potentially carcinogenic); extremely inadvisable			Novidium®, Ethidium®
IM : intra-muscular		IV : intra-veinous		SC : sub-cutaneous	

Curative treatment

Curative treatment aims at eliminating all parasites in a sick animal. The quantity of drug used could be regarded as a "sterilising" dose. Consequently in ruminants a curative dose of diminazene aceturate is injected intramuscularly (picture 4) to obtain a high concentration of the active ingredient in the circulating blood. The withdrawal period for the consumption of meat of cattle injected with trypanocides is 21 days; no period has been indicated for milk but at least 3 days should be taken into account since the product is also found in milk.

- Cattle and small ruminant trypanosomosis: use diminazene aceturate (drug of choice) at the dose of 7 mg/kg. If the treatment proves not to be effective it is recommended to use isometamidium chloride at the dose of 0.5 mg/kg (withdrawal period for the consumption of meat from treated animals is 30 days).

- Equine trypanosomosis:

- In *Trypanosoma vivax* or *T.congolense*: treat with isometamidium intravenously (dose to be divided up in horse);
- In *T. brucei* or *T. evansi*: use melarsamine, quinapyramine or suramine ;
- In any clinical case a dose of 7 mg/kg of diminazene aceturate can be used but the injection must be given in divided doses.

- Camel trypanosomosis: in *T. evansi* infection, melarsamine is the ideal product (dose: 0.25 mg/kg), but a dose of 3.5 mg/kg of diminazene aceturate can also be used (note: can give severe side-effects).

- Pig trypanosomosis: in *T. simiae* : use quinapyramine.



Picture 4. Intra-muscular injection.
(photo M. Desquesnes)

Preventive Treatment

Isometamidium chloride

Preventive treatment is also called chemoprophylaxis or chemoprevention, and is used to protect healthy animals (or possibly infected) against infections during a period equal to the duration of protection of the product at the recommended dosage. Isometamidium chloride is the main drug which, depending on the dose administered, from 0.5 to 1 mg/kg , ensures a protection from 2 to 4 months. The injection must be done by deep intramuscular injection.

- For cattle on transhumance in high risk areas (picture 5), treatment with isometamidium must be done the day before departures. This will guarantee a protection from 2 to 4 months, depending on the dose used. As soon as they return, all animals must be treated with diminazene aceturate in order to eliminate possible strains resistant to isometamidium and the infections contracted during transhumance .

- For cattle meant for meat production, walking across infested zones, isometamidium chloride at the dose of 0.5 mg /kg ensures sufficient protection but the time allowed to wait before consumption of the meat should be taken into account: (30 days) .

- For milking cows or sensitive animals (zebus) living in high risk zones protection should be given every 4 months with isometamidium (1 mg/kg) and at least once a year with diminazene aceturate. If the risk is low, isometamidium will be used only during the high risk period .

- In trypanotolerant young bulls bred in their region of origin, chemoprevention is not advised . If they are newly introduced in regions with a high trypanosomosis incidence, it is advised to treat them with diminazene aceturate when they arrive (7 mg/kg), and a week later with isometamidium (0.5 mg/kg).

- For small ruminants, isometamidium (0.5-1 mg /kg) allows a protection from 2 to 4 months .



Picture 5. During transhumance the risk is often high
(photo M. Desquesnes)

- In equines isometamidium (0.5-1 mg/kg) can be used, provided it is given in divided doses. In zones in which *T. evansi* occurs, quinapyramine prosalt can be used. The duration of protection is then from about 2 to 3 months.
- Camels can be treated with isometamidium chloride (0.5-1mg/kg). However they are sensitive to the product when the dosage reaches 1 mg/kg. Quinapyramine prosalt can also be used.

In general preventive treatments tend to select resistant strains because of their slow elimination; it is therefore very important to respect the period of time between two treatments and to ensure that curative treatment is given using a trypanocide of a different chemical category (diminazene aceturate for example).

Diminazene Aceturate

Another preventive treatment technique consists of applying in a repeated way diminazene aceturate at a dose of 3.5 mg/kg, about once a month. In this case it can be administered by

sub-cutaneous injection (picture 6). This technique offers the advantage of immunising animals, since those treatments reinforce the control of infections without eliminating them totally (carrier immunity). The period of time between 2 treatments does not allow parasites to provoke serious disease. It is the method of choice for controlling trypanosomes in a highly enzootic environment with resistant or fairly resistant cattle. It must be used only during high-risk periods else it would also favour chemoresistance .



Picture 6. Sub-cutaneous injection.
(photo M. Desquesnes)

Strategic use of trypanocides

The strategic use of trypanocides must be defined depending on the importance and the seasonal character of trypanosomosis risk as well as the degree of trypanotolerance of the animals.

Low risk all-year-round

A chemoprophylactic treatment is not necessary; it is recommended to give curative treatment only to infected or sick animals with diminazene aceturate (7 mg/kg). This situation concerns areas of low trypanosomosis risk where zebus are the predominant breed (picture 7).



Picture 7. Zebu cattle trypanosensitive.
(photo Y. Lombo)

High risk during a certain period of the year.

For many countries the risk period is at the end of rainy season until the beginning of the cold dry season. Therefore two weeks before the end of the cold season (harmattan), all sensitive cattle should be treated with isometamidium chloride (picture 8), and more resistant cattle in a repeated way with diminazene aceturate (3.5 mg/kg), thus creating protection during the high risk period. Outside this period, newly detected cases should be treated (curative) with diminazene aceturete (7 mg/kg).



Picture 8. Cattle with predominant zebu characteristics (trypanosensitive).
(photo M. Desquesnes)

High trypanosomosis risk all-year-round

In those areas breeding of trypanotolerant breeds or trypanotolerant cross-breeds is common practice (picture 9 and 10). However in some cases when parasite pressure is very high even trypanotolerant cattle must receive prophylactic treatment. In high risk areas sensitive animals, milking cows, and breeding zebu bulls need preventive treatment (picture 10).

An annual program of chemoprophylaxis can be applied to the whole herd. Animals must receive quite a continuous protection either by repeated treatment at one month intervals with diminazene aceturate (3.5mg /kg) in trypanotolerant cattle or by a continuous protection with isometamidium chloride administered every 3 months at the dose of 1 mg/kg in sensitive cattle. In all cases treatment with isometamidium and diminazene should be alternated at least once a year to eliminate resistant strains produced by the haphazard alternation of trypanocides. To do so, treatment with diminazene aceturate (7 mg/kg) should be administered and 15 days later chemoprophylactic treatment with isometamidium chloride (1 mg /kg) should be started and done every 3 month.



Picture 9. Cattle with predominant baoule characteristics (trypanotolerant)
(photo M. Desquesnes)



Picture 10. A zebu bull (trypanosensitive) to be protected among somba cows (trypanotolerant) and their cross breed products
(photo M. Desquesnes)

The Chemoresistance Problem

How does It appear?

Trypanocides can cause strains of chemo-resistant trypanosomes to appear. This phenomenon has many causes often linked to the sub-dosage of trypanocides:

- effective concentration is not reached after an excessive dilution of trypanocide;
- for economic reasons people want to treat a high number of cattle with only one package of trypanocide and hence reduce the dose of each treatment;
- a sub-dosage is applied because of under-estimation of the animal's weight;
- the product used is not genuine, and contains a quantity of trypanocide lower than indicated on the package;
- an abscess has formed at the injection site hindering the normal diffusion of the drug;
- a very long interval of time has been allowed between 2 chemo-preventive treatments.

In any of these cases trypanosomes are exposed to low doses of the product which allows the most resistant individuals to survive. After many generations of parasites and possible hybridisation in tsetse flies, highly resistant trypanosomosis strains can appear. Those strains happen to be resistant to two or three times the recommended dose of the product. In such situations nothing can eliminate them, except through a change of chemical category of trypanocide.



Picture 11. Treating without weight estimation: a wrong practice. (photo M. L. Dia)

Since we have in practice only 2 trypanocidal chemical categories, the likely appearance of strains resistant to those 2 products should be avoided.

What are the contra-indicated products ?

Ethidium derivatives can, beside their innate toxicity, cause resistance to two other trypanocides (diminazene and isometamidium); for this additional reason, this product must be strictly prohibited from veterinary use.

Quinapyramine derivatives can favour multiple resistance to three other trypanocides (diminazene, isometamidium and ethidium). Their use must therefore be avoided for ruminants.

When should chemoresistance be suspected ?

When treatment has no satisfactory clinical effect. In those cases, trypanocides must be alternated : resistance to diminazene should be treated with isometamidium and the one due to isometamidium with diminazene. Resistance to suramine may be overcome with melarsamine and the one to quinapyramine prosalt with suramine.

In case of multiple resistance, report the veterinary services and contact CIRDES to set up a control policy adapted to the situation.

Some practical advices

- The diagnosis of trypanosomiasis should be done by a veterinarian and, as far as possible confirmed by microscopic examination. Knowledge of the haematocrit value of the animal can improve prognosis.
- The weight of animals to be treated must be known through weighing, or estimated with a barymetric tape (correspondence between thoracic perimeter and the live weight of the animal) (picture 12) or from a good experience in weight estimation by visual inspection.
- Preferably the trypanocide should be administered just after their reconstitution. Sub-cutaneous injection is done at neck level behind the shoulder, or at dewlap level. Preferably intramuscular injection is done in the third upper part; and the intravenous one at the jugular vein level.
- Use of Berenil®: There are individual packages of 2.36g and collective packages of 23.6g. The individual package is reconstituted in 15 ml of water and allows a curative treatment of 150kg of cattle (dose of 7 mg/kg) or, when it is used as a preventive treatment in a repeated way, 300 kg of cattle (dose of 3.5 mg/kg as indicated on the package). The collective package is reconstituted in 150 ml of water. It allows the treatment of 10 times as many cattle. It should be noted that the dose indicated by the manufacturer is the lower dose (3.5mg/kg) which, in most cases, is unable to eliminate parasites. A curative treatment requires a double dose of 7mg/kg.
- Use of trypanamidium®: the package of 1 g should be diluted in 100 ml of water. As a preventive treatment, it should be

given at a dose of 1 ml for 10 kg of lively weight. When trypanamidium® is used as a curative treatment (alternately with dimazene aceturate for instance), the dose of 0.5 mg/kg that is 1 ml for 20kg of live weight is applied.

- In all cases, when one of those products is mostly used, it is recommended to use the other product with curative dose at least once a year, in order to suppress susceptible resistant strains.
- It is always advised to improve the condition of animals by giving symptomatic treatment.



Picture 12. barymetry for weight estimation.
(photo M. Desquesnes)

Beware of fake drugs !

Fake trypanocides are widely sold in West Africa. The drugs are either fake in their composition or are faked by dilution of the original product or by substitution by an ordinary component apparently alike (Nere powder for Berenil®, Coffee or Charcoal, for Ethidium, Potassium permanganate for isometamidium, etc.). For Trypanamidium®, one must pay attention to the information given on the packages (the example of a shell

found on a fake product labelled: "for veterinary use"), and in general carefully check the logo of firms, etc. in order to tell the fake from the original one.

Seek advice from recognised veterinarians, use well-known products, and be a regular customer to a trustworthy supply service.

To sum up.

To effectively treat trypanosomosis, it is better to identify animals to be treated and it is necessary to use the curative dose.

To ensure an effective prophylactic treatment, it is compulsory to know the epidemiological situation of the area and the distance covered by animals (transhumance). This allows the development of chemo-prophylactic programmes which can only be effective when all the animals of the herd are treated without exception and also when the prophylactic timing is respected; that is, the interval of time between two infections.

In all cases it is essential to:

- get supplies of trypanocides from an accredited source;
- estimate or measure the animal's weight in a reliable way;
- sterile material for injections should only be used once;
- do not try to economise on drugs by under-dosing.



Picture 13. Non sterile material, single needle for the whole herd: a wrong practice to avoid. (photo M.L. Dia)

To know more

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➔ *This technical note is destined to decision makers, veterinarians and breeding technicians. The last being in charge of bringing the message to the farmers.*

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