

RESEARCH COMMUNICATION

THE INFLUENCE OF DITHIOSEMICARBAZONE* ON THE IMMUNITY OF SHEEP TO HEARTWATER

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ABSTRACT

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Four out of 9 sheep, immune to heartwater and subsequently treated with gloxazone, showed a febrile reaction when they were challenged 6 months later, but the same number of untreated controls also developed this reaction. In a second group of treated immune animals challenged after 9 months, 8 out of 8 showed a febrile reaction, whereas only 3 out of 8 controls reacted. Furthermore, the blood of one of the 4 sheep that reacted to challenge at 6 months was infective to a susceptible sheep inoculated with it, whereas that of 4 out of the 8 challenged at 9 months was infective.

Résumé

L'INFLUENCE DU DITHIOSEMICARBAZONE SUR L'IMMUNITÉ DU MOUTON À LA COWDRIOSE

Quatre sur neuf moutons immuns à la cowdriose (infection à *Cowdria ruminantium*) et ultérieurement traités au gloxazone, ont montré une réaction fébrile quand ils furent éprouvés six mois plus tard à une infection à *C. ruminantium*, mais le même nombre de témoins non traités développèrent aussi cette réaction. Dans un second groupe d'animaux immuns traités, après neuf mois, 3 sur 8 montrèrent une réaction fébrile, tandis que trois des huit témoins réagirent. De plus, le sang d'un des quatre moutons qui avaient réagi à l'épreuve à six mois fut infectieux pour un mouton susceptible inoculé avec lui, tandis que quatre des huit éprouvés à neuf mois étaient infectieux.

INTRODUCTION

The mechanism of immunity in heartwater is obscure. Preliminary results suggested that it is probably not dependent on serum antibodies, but rather that it is cell-mediated (Du Plessis, 1970).

The immunity of mice to the mouse strain of *Cowdria ruminantium* is characterized by persistence of the agent in the tissues of the mice (Du Plessis, 1981). A latent infection such as this in mice can be successfully treated with gloxazone.

Since a latent infection is an important feature of the immunity to other rickettsia-like agents such as *Ehrlichia phagocytophila* (Foggie, 1951), *Ehrlichia canis* (Donatien & Lestoquard, 1937) and *Cytocetes ondiri* (Snodgrass, 1975), it was decided to attempt to sterilize sheep immune to heartwater by the administration of gloxazone and then to challenge them.

MATERIALS AND METHODS

Thirty-six 6-12-month-old Merino ewes were immunized against the Ball 3 strain of *C. ruminantium* as previously described (Du Plessis, 1981). One to 2 months after their recovery from the artificial infection, 18 of the sheep were injected intramuscularly on 3 consecutive days with gloxazone at a dosage level of 10 mg/kg body mass and the other 18 left untreated as controls.

Six months later, 9 gloxazone-treated and 9 control sheep were challenged with virulent Ball 3 strain *C. ruminantium*-infected sheep's blood. Ten ml of heparinized blood, drawn from each of the animals that reacted to the challenge on the 2nd day of the febrile reaction, was inoculated into a susceptible sheep. Nine months after they had been treated with gloxazone, the procedure was repeated with the other 8 gloxazone-treated sheep† and an equal number of controls.

* Gloxazone, Coopers (Wellcome)

† One sheep had died from kidney failure as a result of the treatment

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RESULTS

Table 1 shows that 4 out of 9 gloxazone-treated immune sheep showed febrile reactions of varying severity when they were challenged with virulent heartwater blood 6 months later. The same number of control immune sheep showed similar reactions when they were challenged. The blood from 1 of the 4 gloxazone-treated sheep that reacted to the challenge and that from 1 of the 4 controls elicited severe reactions in sheep inoculated with it, and in 1 case death resulted.

TABLE 1 The influence of gloxazone on the immunity of sheep to heartwater

Months after gloxazone treatment	Parameters at challenge	Gloxazone-treated	Controls
6	Febrile reaction	4/9 ⁽¹⁾	4/9
	Sub-inoculation	1/4 ⁽²⁾	1/4
9	Febrile reaction	8/8	3/8
	Sub-inoculation	4/8	1/3

⁽¹⁾ Four out of 9 sheep showed a febrile reaction when they were challenged

⁽²⁾ One out of 4 susceptible sheep inoculated with blood from the 4 sheep in (1) reacted or died

At 9 months after gloxazone-treatment, however, 8 out of 8 treated sheep showed febrile reactions as against 3 out of 8 controls. Furthermore, the blood from 4 out of the 8 gloxazone-treated animals that reacted was infective, whereas that from only 1 of the 3 control sheep that reacted was infective.

DISCUSSION

It would appear that sheep, immune to heartwater and subsequently drug-sterilized, were less resistant to challenge 9 months later than infected control sheep. The difference between treated immune sheep and untreated controls was not apparent at 6 months, possibly because the effects of a latent infection, mediated by the cellular defence of the body, persist for 6 months after disappearance of the agent, but not for as long as 9 months.

The small number of sheep used does not warrant any definite conclusions, but these preliminary findings suggest that the resistance to challenge of sheep immune to heartwater possibly depends on the persistence of the agent in the tissues of the sheep. This finding is in accordance with that of the immune status of mice that recovered from infection with the mouse strain of *C. ruminantium*. Here it was found

that the agent could be detected in the tissues of mice over almost the entire course of the 18 months during which they were found to be immune (Du Plessis, 1981).

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