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2	disease problem in pastoral communities
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Abstract:

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A neurological syndrome of small ruminants, known locally as 'ormilo', has been reported amongst pastoralist livestock keepers in Tanzania. This study was carried out in four affected pastoral communities to determine the prevalence and associated risk factors, characterise the clinical signs and investigate the aetiology of the syndrome. Questionnaires were administered at all households (n=480) within four study villages. Overall, 94% of households reported at least one case in the previous 12 months. By village, the individual-level 12-month period prevalence ranged from 11-34%, equivalent to about 10,000 small ruminants across the four Thirty-eight households were randomly selected for further investigation. Proprioceptive deficits and weakness were the most commonly observed clinical signs in affected animals. Brain and spinal cord cysts consistent with Taenia multiceps infection were detected in 32 (82%) of 39 affected animals selected for post-mortem examination. Feeding small ruminant brains to dogs was identified as an important risk factor for the syndrome, even in households that did not own dogs. This study confirms cerebral coenurosis as a major cause of small ruminant neurological disease in northern Tanzania and highlights the urgent need for further investigation to quantify the disease burden and to identify and implement control measures.

Introduction

A neurological syndrome known locally as 'ormilo', is reported to be emerging as a major health problem of small ruminants in pastoral livestock settings in northern Tanzania (1). However, little is known about the aetiology of this syndrome, preventing the development of effective control strategies. Differential diagnoses for neurological disease in small ruminants in tropical areas are varied and include bacterial infections such as listeriosis (*Listeria monocytogenes*) and heartwater (*Ehrlichia ruminantium*) (2), viruses such as rabies and maedi-visna, and parasitic infections such as cerebral coenurosis (*Taenia multiceps*), as well as non-infectious causes including nutritional deficiencies (e.g. thiamine deficiency) and toxin ingestion (3). In Tanzania, a recent abattoir study detected cerebral coenurosis in 44% small ruminants brought for slaughter in Ngorongoro District (4), suggesting this may be an important cause of neurological disease in this area. However, animals presented for slaughter may not be representative of the wider population, and further investigation is needed to understand the prevalence of this disease.

Epidemiological data for cerebral coenurosis is limited in Africa but the disease is thought to occur in small ruminant production systems across the continent (5). Cerebral coenurosis, also known as "gid", is a progressive neurological disease of sheep and goats, caused by infection with the metacestode stage of the canine tapeworm, *T. multiceps*, a cestode parasite with an indirect life cycle and a worldwide distribution (5). The definitive host is the domestic dog, with adult cestodes inhabiting the canine small intestine and gravid proglottid segments shed into the environment in faecal matter. Following ingestion of embryonated eggs by small ruminants from contaminated pastures, larvae burrow through the intestinal wall and are transported to predilection sites including the brain and spinal cord, where they form cysts, known as coenuri. Clinical signs occur in two phases: firstly, in association with larval migration and acute inflammation in the brain, and secondly, progressive clinical signs are seen as coenurus cysts enlarge over time (5-8). The condition is typically fatal, resulting in direct losses to small ruminant keepers and imposing a significant burden on small ruminant production (9).

Sheep and goat production is increasingly important to pastoral communities in East Africa that are highly dependent on livestock for household income and food security. A shift towards keeping small ruminants rather than cattle has been reported in response to a complex array of environmental, economic and social challenges, reflecting not only market forces but the greater resilience of sheep and goats in the face of a changing climate, increasing drought

frequency and pasture shortages (10-12). Causes of production loss in these species can therefore present an important threat to pastoralist livelihoods and food security (13). In recent surveys conducted as part of participatory community-based studies of zoonotic livestock diseases in northern Tanzania (14), pastoral livestock-keepers expressed high levels of concern about neurological abnormalities in small ruminants and identified this syndrome as the leading animal health concern. In response to these findings, this study was established to: (a) determine the reported 12-month period prevalence and point prevalence of the neurological syndrome in sheep and goats kept by pastoral communities in northern Tanzania; (b) characterise the clinical presentation; (c) investigate the contribution of *T. multiceps* infection and (d) identify risk factors associated with the syndrome.

Materials and methods

Study area

The study was carried out in the Arusha region of northern Tanzania between January and March 2018. The region consists of semi-arid and sub-tropical areas and is divided into seven administrative districts. Study villages were located in Longido and Monduli Districts (Figure 1), where livestock keepers operate predominantly extensive pastoralist grazing systems for livestock. Study villages were identified from randomly-selected villages (n = 20) participating in earlier research studies on zoonoses in emerging livestock systems (BBSRC BB/L018926/1) (14). Four villages were selected for further investigation based on previously reported cases of the neurological syndrome, ease of access and good working relationships with local livestock field officers.

Ethical clearance

- Research clearance for this study was granted by the Tanzania Commission for Science and
- Technology (No. 2018-48-NA-2005-141) and ethical clearance by the University of Glasgow
- 114 School of Veterinary Medicine Ethics Committee (REF 43a/17). Informed written consent for
- livestock examination and sampling was obtained from the head of each household.

Study design

- questionnaire survey was administered at all households in each of the four villages to (i)
- quantify farmer-reported 12-month period prevalence and point prevalence of the neurological
- syndrome in sheep and goats and (ii) to collect data to identify potential risk factors for the

The study comprised a cross-sectional survey consisting of three elements. Firstly, a

syndrome, including flock size, dog ownership and dog feeding practices. Questionnaires were administered to the head of each household by local livestock field officers in Kiswahili following training and pilot testing.

Secondly, a target of ten households reporting current cases of neurological syndrome in small ruminants were randomly selected per village for further investigation. At each selected household farmers were asked to identify all animals currently affected with the neurological syndrome. All identified cases were examined by a veterinarian to document clinical signs associated with the syndrome, including assessment of mentation, posture, gait, proprioception and cranial nerve function using standard clinical approaches described in the veterinary neurology literature (15; 16).

Thirdly, a subset of affected animals were selected for post-mortem examination. Numbers were assigned to affected animals identified by the farmer as destined for slaughter. Up to two animals from each household were selected at random by drawing numbers from a hat. Farmers were compensated for the market value of each selected animal. Animals were then humanely slaughtered by trained livestock officers following international guidelines for slaughter of small ruminant livestock for human consumption (17; 18) At post-mortem examination, the brain and spinal cord were removed from each animal and examined for evidence of gross pathology. Where cysts were identified, sections of cyst wall and protoscoleces were collected into 70% ethanol for DNA preservation and subsequent molecular testing.

Laboratory diagnosis

PCR-based amplification and sequencing of a ~470bp fragment of the *Taenia* NADH-1 mitochondrial gene was performed to determine the presence of *T. multiceps* and confirm the diagnosis of coenurosis in animals with brain or spinal cord cysts (19; 20). DNA was extracted from cysts preserved in ethanol using the QIAamp DNA Mini Kit spin-column protocol for DNA purification from tissues (Qiagen, Maryland, USA). PCR assays were performed following previously published protocols designed for molecular speciation of *Taenia* infections (19; 20). PCR amplicons were sequenced and compared to published sequences using the BLAST nucleotide alignment search tool available in GenBank to confirm the infecting *Taenia* species (21).

Data analysis

Maps of the study area were made using QGIS open access software (version 2.18). National, regional and village-level shape files were obtained from Tanzania National Bureau of Statistics (22). Statistical analyses were performed in R statistical environment, version 3.4.4 (http://cran.r-project.org/). Household and individual-level point prevalence was determined as the proportion of households or individual animals affected at the time of the survey. Due to the reported high turnover of affected animals, 12-month period prevalence was also calculated to provide a more robust estimate of the scale and impact of the problem. Household 12-month period prevalence was calculated as the number of households with at least one reported case in the last year divided by the total number of households. Individual 12-month period prevalence was calculated as the number of animals reported to be affected, over the current flock size, assuming a stable flock size over the same period. Prevalence estimates were calculated for small ruminants as a unit because sheep and goats are typically managed together in this setting, and also by species, to look for differences in susceptibility to the syndrome.

Statistical significance was set at a value of p≤0.05. Pearson's chi-squared tests were used to evaluate the difference in point prevalence and 12-month period prevalence between sheep and goats. Regression analysis was performed to investigate risk factors associated with the count of cases at the household over the past 12 months. Explanatory variables included the natural logarithm of flock size, village, dog ownership (yes or no), whether farmers reported feeding small ruminant brains to dogs (yes or no) and an interaction term between dog ownership and brain-feeding. Two models were constructed; firstly, a Poisson regression model for count data and secondly a negative binomial model to account for over-dispersal in the data. Goodness of fit for the two models with and without the addition of the interaction term, was evaluated using a likelihood ratio test.

Results

Descriptive data

Questionnaires were administered at 480 households across the four villages. Village size ranged from 83 to 157 households and between approximately 6,000 and 17,000 small ruminants were kept per village. Of the 480 households, 474 (98.8%) currently kept small ruminants and 374 (77.9%) kept at least one dog. Sheep accounted for 58.0% of all small ruminants kept.

12-month period prevalence and point prevalence

In total, 445 (93.9%) of the 474 small ruminant-keeping households had experienced at least one case of neurological syndrome in sheep or goats in the last 12 months (Table 1). By village, between 10.9% and 34.0% of small ruminants in each village were reported to have been affected during the same period (Table 1). Overall, the individual-level 12-month period prevalence was significantly higher in goats than sheep ($\chi^2=26.6$, d.f.=1, p<0.001).

Table 1: 12-month period prevalence (household and individual) of farmer-reported neurological syndrome in sheep and goats in northern Tanzania

	Number of small ruminant-keeping households reporting ≥ one case of neurological	Reported number of animals affected in the previous 12 months (individual 12-month period prevalence %)		
Village	syndrome in sheep or	Sheep	Goats	Total
	N (%)	N (%)	N (%)	N (%)
1	140 (91.5)	3043 (24.9)	1990 (39.2)	5033 (29.1)
2	115 (96.6)	1195 (33.4)	970 (34.8)	2165 (34.0)
3	83 (100.0)	1220 (28.0)	1287 (19.8)	2507 (23.1)
4	107 (89.9)	504 (9.9)	475 (12.1)	979 (10.9)
Total	445 (93.9)	5962 (23.6)	4722 (25.8)	10684 (24.6)

At the time of the survey, 51.1% of small ruminant-keeping households reported current cases of neurological syndrome in sheep and goats (Table 2). By village, between 0.9% and 2.9% of small ruminants were reported to be currently affected with neurological syndrome (Table 2). No significance difference was detected in point prevalence between small ruminant species.

Table 2: Point prevalence (household and individual) of farmer-reported neurological syndrome in sheep and goats in northern Tanzania

	Number of small	Reported number of animals affected at the time			
	ruminant-keeping	of survey			
	households	(individual point prevalenc		ence %)	
	reporting cases of				
X7211	neurological	Sheep Goat		Total	
Village	syndrome at the		Goat		
	time of survey				
	(household point				
	prevalence)				
	N (%)	N (%)	N (%)	N (%)	
1	103 (67.3%)	320 (2.6)	180 (3.5)	500 (2.9)	
2	55 (46.2)	81 (2.3)	76 (2.7)	157 (2.5)	
3	42 (50.6)	103 (2.4)	140 (2.1)	243 (2.2)	
4	42 (35.3)	57 (1.1)	27 (0.7)	84 (0.9)	
Total	242 (51.1)	561 (2.2)	423 (2.3)	984 (2.3)	

Description of affected animals

Across the four villages, 38 households with current cases of neurological syndrome were randomly selected to participate in clinical investigation (10 households in villages 1 & 4; 9 households in villages 2 & 3). In total, 74 animals were reported to be affected at the time of the survey. Reported duration of clinical signs at the time of examination ranged from less than one week (7/74, 9.5%) to 1 year (2/74, 2.7%). Sheep and goats were similarly represented in affected cases (n=36 (48.7%) and n=38 (51.4%) respectively). The reported age of affected animals ranged from two months to seven years old, with the 65.5% (38/58 animals with age data available) of animals recorded as 1 year or under.

Neurological deficits were detected on clinical examination in 73 (98.6%) of the 74 animals with reported neurological syndrome. Observed neurological deficits ranged in severity from subtle gait or proprioceptive abnormalities, to pronounced mentation, postural, gait and cranial nerve deficits (Figure 2). The most commonly observed neurological signs were proprioceptive deficits (n=61, 82.4%); weakness, particularly in the hind limbs (n=55, 74.3%) and gait abnormalities (n=48, 64.9%) which most commonly presented as hindlimb ataxia. Circling was frequently mentioned by farmers but was only observed in 11 animals (14.9%). Functional cranial nerve deficits, including reduced or absent menace, palpebral and pupillary

227 light responses, were observed in 38 animals (51.4%). Mentation was normal in most cases

228 (n=65, 87.8%).

Post mortem examinations and laboratory diagnosis

Post mortem examinations were carried out on 39 animals (20 sheep, 19 goats) that demonstrated neurological deficits on clinical examination. One or more large, focal or multifocal, fluid-filled cystic structures (Figure 3) were detected in the brain (n=30) or spinal cord (n=2) of 32 (82.1%) cases examined. Cysts had a bladder-like appearance, filled with clear fluid and multiple small white protoscoleces (Figure 4), and ranged in size from less than 1cm to more than 4cm in diameter. Cysts were found in all regions of the brain (cerebrum, cerebellum and brain stem) and multiple cysts were found in 40.6% (n=13) of cases. Necrotic tracts were observed in the brain parenchyma adjacent to cysts in some cases. In two animals, a single fluid-filled cyst was detected adjacent to and compressing the spinal cord in the lumbar-sacral and thoraco-lumbar regions, respectively. All cysts had a gross appearance consistent with *T. multiceps* coenuri. *T. multiceps* infection causing coenurosis was confirmed by PCR and sequencing in all cases (n=32) (see GenBank accession numbers for representative sequences generated through this study).

Seven animals showed evidence of neurological deficits but had no evidence of *T. multiceps* coenuri. In one case, hydrocephalus, characterised by distended cerebral ventricles was observed. A second individual had a large, space-occupying cystic structure filled with yellow translucent liquid and surrounded by a wide area of necrotic brain tissue. No evidence of protoscoleces was seen in this cyst, which was also negative by *T. multiceps* PCR. Fly larvae were detected in the frontal sinuses of a third animal. No gross pathology was evident in the remaining four cases.

Statistical analysis

Regression analysis was performed to identify risk factors for neurological syndrome in small ruminants in our study villages. A restricted dataset was used that excluded non-livestock owning households and households with missing values for number of cases seen in the last 12 months, resulting in a dataset with 467 households. A negative binomial regression model including an interaction between dog ownership and feeding brains to dogs provided the best fit to the data. The final model demonstrated that flock size, dog ownership, feeding brains to dogs, and village were significantly associated with the number of cases of neurological syndrome reported in small ruminants in the previous 12-months (Table 3).

Table 3: Rate ratios, 95% confidence intervals and P values for explanatory variables in final negative binomial regression model for neurological syndrome in small ruminants

Variable	Rate ratio	P value
	(95% confidence intervals)	
(Intercept)	1.1 (0.70-1.73)	0.676
Dog ownership	2.0 (1.26-3.08)	0.003
Feed brains to dogs	2.6 (1.71-3.81)	< 0.001
Log (flock size)	1.7 (1.58-1.84)	< 0.001
Village 1	Baseline	
Village 2	0.7 (0.59-0.86)	< 0.001
Village 3	0.8 (0.67-1.01)	0.057
Village 4	0.3 (0.26-0.38)	< 0.001
Dog ownership*Feed brains	0.6 (0.37-0.97)	0.036
to dogs		

Across all households, a large proportion of respondents (n=383, 79.8%) reported having fed sheep or goat brains to dogs, including in 65 (61.3%) out of 106 households that did not own dogs. Both dog ownership and the practice of brain-feeding were statistically significant, but the effect for each of these two variables modified that of the other. The greatest risk of neurological syndrome was associated with households that both owned dogs and fed brains, when compared to households that did neither (rate ratio 3 (95% CI 2.1 – 4.4), estimated from the regression co-efficients (β) derived from the model shown in Table 3, i.e. β fed + β own + β own*fed). However, even in households that did not own dogs, the practice of brain-feeding alone was associated with a rate ratio of 2.6 (95% CI 1.7 – 3.8). In households that did not report brain-feeding, owning dogs was associated with a rate ratio of 2.0 (95% CI 1.3 – 3.1), whereas in households that fed brains to dogs, owning dogs was associated with a small, non-significant increase in risk (rate ratio 1.17 (95% CI 0.95 – 1.45), β own dogs + β own dogs*fed dogs).

Discussion

Our study, investigating the problem of a severe neurological syndrome in small ruminants in pastoral communities of northern Tanzania, demonstrates several key findings. Firstly,

neurological abnormalities are widely reported in small ruminants in our study villages with almost all flocks (94%) affected. The individual-level 12-month period prevalence is also high, with 11-34% of sheep and goats in each village reported to have been affected over the last year. Secondly, post mortem findings revealed that cerebral coenurosis is a major contributing cause of this neurological syndrome in sheep and goats in these villages, with brain cysts detected in 82% of clinically-affected animals and *T. multiceps* confirmed through PCR and sequencing. Finally, our risk factor analysis identified dog ownership and the practice of feeding small ruminant brains to dogs as significant risk factors for this neurological syndrome. Our study provides important insights into the prevalence and aetiology of neurological disease in sheep and goats in this area and identifies risk factors that could be targeted to help control this important animal health problem.

Period prevalence estimates obtained from this study indicate that the neurological syndrome reported by farmers is common and poses a major burden for small ruminant production in this setting. Although the point prevalence of neurological syndrome reported in our study (2.3%) is relatively low, point prevalence estimates are limited, as the rapid sale or slaughter of affected animals reported in our system means that point prevalence is likely to be highly dynamic and therefore may not be representative of the true scale of the problem. The use of 12-month period prevalence in our study allowed us to improve our estimates of losses and highlighted the scale of the problem over time. In this small-scale study of four villages, almost 10,000 small ruminants were reported to be affected by this neurological syndrome over a 12-month period. Given the typically fatal outcome of the syndrome, both directly (e.g. through death or predation) and via premature slaughter of affected animals resulting in a loss of market value, this syndrome is resulting in substantial financial and production losses for livestock-dependent communities in northern Tanzania.

Cerebral coenurosis appears to be a major contributing cause of the neurological syndrome of small ruminants reported in northern Tanzania. Evidence of *T. multiceps* coenuri were found in more than 80% of cases at post mortem examination and clinical signs were consistent with those reported in outbreaks of cerebral coenurosis described elsewhere (23-25). Further investigations, such as histopathology on brain tissue or testing for other infectious agents, were not performed as part of this study hence other causes of neurological disease could not be ruled out. However, gross pathology is considered pathognomonic for the diagnosis of cerebral coenurosis in the presence of compatible clinical signs.

In our study, the majority of affected animals were one year old or less which is consistent with reports in the literature (9; 26). Infection was also seen in several animals under 6 months, including a two-month old lamb that had several small multifocal parasitic cysts scattered on the cerebral surface and necrotic tracts in the cerebral tissue. The very young age of some of the animals in our study was surprising as the interval between infection and onset of clinical signs has previously been estimated as two to six months (25) and maternally derived antibodies could be expected to still provide protection at this age (27; 28). Early onset cases have been described where naïve animals have been exposed to a very high burden of *T. multiceps* eggs, but appear to be rare (24; 29). In these cases progression to clinical signs, and even death, can occur in less than a week (30). It remains unclear whether the young age profile seen in this study reflects a particularly high environmental burden of *T. multiceps*, intrinsic host factors such as immuno-compromise, or pathogen strain characteristics, and further work is needed to understand the early onset of disease in this setting.

Dog ownership and the practice of feeding livestock brains to dogs were both identified as significant risk factors for reported cases of neurological syndrome, which is consistent with our conclusion that cerebral coenurosis is a major cause of neurological disease in small ruminants in our study area. Feeding brains of small ruminants to dogs is a common practice, reported by 79.8% of households in this study and observed elsewhere in northern Tanzania (1,2). Our results show that disease risk is more strongly associated with brain-feeding behaviour than dog ownership per se suggesting that preventing this behaviour may be more important than changing dog ownership practices in affected communities. Education and changing behavioural practices related to the disposal of infected offal, which have been important elements in *T. multiceps* control and prevention elsewhere (25), could therefore be highly effective in these communities. Other preventive measures could be considered in combination with behavioural interventions, include anthelminthic (praziquantel) treatment of dogs, which is an important mainstay of control programmes in other parts of the world and can also be used to control other zoonotic cestode parasites such as Echinococcus granulosis, which is also reported in livestock in northern Tanzania (31). Our results emphasise that intervention strategies, especially behavioural interventions, will need to engage the whole community, not only dog owners, to encourage the collective action needed to break transmission cycles.

The study presented here was conducted as an initial investigation as such is limited in scope, with only four purposely-selected pastoral study sites. The data presented in this study was

dependent upon farmer reporting, which may have introduced bias into the selection of cases for further investigation. Furthermore, the extent of this disease problem in other livestock-keeping communities in Tanzania, or indeed elsewhere in East Africa, remains unclear and is an important question for further investigation. Previous research in Tanzania has shown that dogs kept in pastoralist households are more likely to carry *Taenia* spp. cestodes than those in agro-pastoralist households (22), suggesting that sheep and goats kept by pastoral communities may be at higher risk of disease than in other farming systems. Further work is needed to understand the extent to which this disease problem is occurring elsewhere in Tanzania and to characterise the burden of small ruminant neurological disease in different farming systems.

It is also unclear whether the high prevalence of coenurosis detected in this study represents an emerging disease problem in Tanzania or whether the extent of the problem has only recently become apparent as a result of detailed participatory and community-studies carried out as part of other livestock disease research (14). Although coenurosis has previously been highlighted as a concern in pastoral communities of Ngorongoro District in Tanzania (4) and in Ethiopia (9; 32), the disease is rarely prioritised by national veterinary services or international animal health agencies and surveillance data is lacking to compare temporal trends in disease patterns. However, the scale of the problem identified by this study raises urgent questions about the economic, health and social impacts of coenurosis in these communities, as well as the sustainability of livestock-based livelihoods in the East African region in the face of such sustained losses. The issue is particularly acute in the wake of a recent succession of droughts, with the disease posing an additional threat to the small ruminant production base on which pastoralists increasingly depend for food security and survival (11; 12; 33; 34).

Human disease surveillance is also important as *T. multiceps* is a potentially zoonotic infection and may be of particular concern in livestock-dependent communities with limited access to health care. Zoonotic cases of cerebral coenurosis, although rare, have been reported in North America, Europe and the Middle East (35-37) and may occur alongside another zoonotic cestode infection, *E. granulosus*, the cause of human hydatid disease (cystic echinococcosis). Hydatid disease, which has a similar lifecycle to *T. multiceps* with dogs as the definitive host and livestock as the intermediate host, is recognised as an important zoonotic disease problem in pastoralist communities in East Africa (38). It is possible that the factors driving the high prevalence of cerebral coenurosis in small ruminants may also drive a concurrent increase in zoonotic cestode infections in humans. Progression of *E. granulosus* cysts in people is generally much longer (months to years) (39) than the progression of *T. multiceps* coenuri in

sheep and goats so an increase in human disease may not be immediately apparent. Therefore, public health authorities should be aware of the risk of human coenurosis and other cestode infections such as cystic echinococcosis as emerging health problems in pastoral communities. Improved surveillance of both animal and human health is recommended to monitor the burden and to identify potential drivers of these two important parasitic infections.

Conclusion

This study indicates that cerebral coenurosis is a predominant cause of a neurological syndrome of small ruminants commonly reported in pastoral communities in northern Tanzania. The point and 12-month period prevalence of farmer-reported cases demonstrates that *T. multiceps* coenurosis, although rarely mentioned as a national veterinary priority, is a major disease of small ruminants in the region. Further work is needed to better quantify the prevalence and incidence of the disease at a wider scale, to understand the economic and social impacts on livestock-keeping communities, and to identify and implement appropriate measures for disease control and prevention.

405 Figures

 Figure 1: Map showing Arusha region with (inset) study village locations. Maps made using QGIS open access software (version 2.18). Shape files were obtained from Tanzania National Bureau of Statistics.

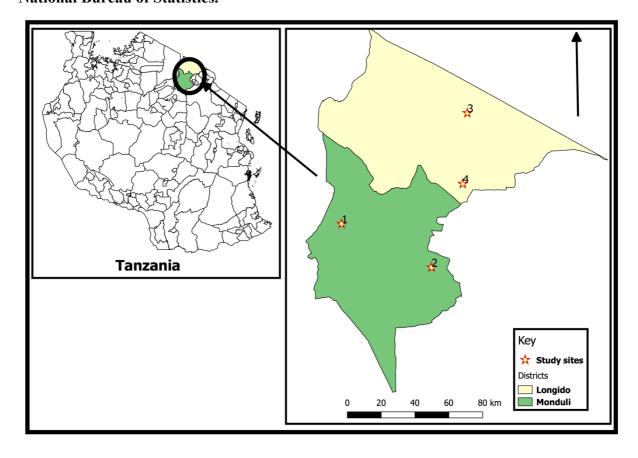


Figure 2: Percentage of affected animals showing different neurological abnormalities.

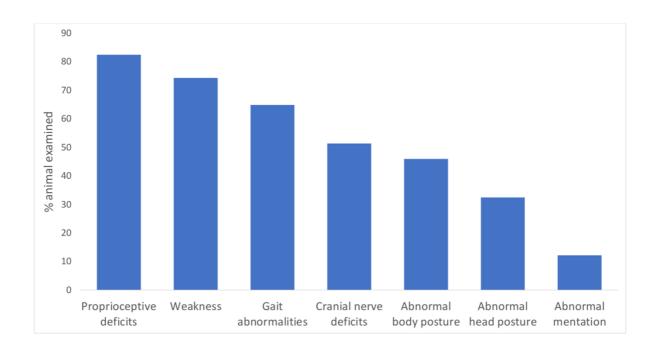


Figure 3: Brain of a goat with multiple fluid-filled cysts and evidence of associated cerebral parenchymal loss.

Figure 4: Cyst removed from the brain of a sheep, showing multiple protoscoleces consistent with *Taenia multiceps* coenurus.



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