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Studies on heterologous immunity in schistosomiasis

6. Observations on cross-immunity to *Ornithobilharzia turkestanicum*, *Schistosoma bovis*, *S. mansoni*, and *S. haematobium* in mice, sheep, and cattle in Iran

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Experiments were carried out in mice, cattle, and sheep to investigate the possibility that heterologous immune reactions may occur between the schistosomes prevalent in man and domestic animals in Iran. Immunization with Ornithobilharzia turkestanicum *from cattle produced a considerable degree of immunity in mice against challenge with* Schistosoma bovis, S. haematobium, *and* S. mansoni. *The results of immunizing cattle with* O. turkestanicum, S. bovis, *and* S. haematobium *were even more striking; there was a reduction of 30–40 % in the number of adult worms and a proportionally greater reduction in the tissue egg counts. Sheep developed a less marked immunity. Supplementary experiments on homologous immunity showed that mice developed a considerable degree of immunity against* S. bovis. *The results of the heterologous immunity experiments with* S. haematobium *and* S. bovis *are of particular interest as both parasites often occur in the same area and are often transmitted by the same snail host, man and cattle being exposed to the cercariae of both species simultaneously. The reciprocal immunity produced by these infections may be mutually beneficial in limiting the severity of schistosomiasis in man and domestic animals in the endemic areas.*

Previous papers in this series have demonstrated a significant heterologous immune response between human and animal schistosomes in mice, monkeys, cattle, and sheep (Nelson et al., 1968; Amin et al., 1968; Amin & Nelson, 1969; Hussein et al., 1970; Preston et al., 1972). The purpose of the study reported here was to extend these observations by investigating the heterologous immune reactions between animal and human schistosomes in Iran, with a view to assessing their possible importance in nature. In the preliminary experiments in mice *Ornithobilharzia turkestanicum* was used as an immunizing agent. In subsequent experiments observations were made on cross-immunity to *O. turkestanicum*, *Schistosoma bovis*, and *S. haematobium* in calves and sheep and the levels of immunity produced by both homologous and heterologous systems were compared.

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EXPERIMENTAL MATERIAL

Four species of schistosome were used: the local strains of *O. turkestanicum*, *S. bovis*, and *S. haematobium*, and a Puerto Rican strain of *S. mansoni* for comparison with previous observations by Nelson et al. (1968) and Amin et al. (1968). The calves and sheep were obtained from areas in Iran where there is no schistosomiasis. The mice were 6-week-old T.O. strain albinos.

HETEROLOGOUS IMMUNITY STUDIES IN MICE

Each experiment was separately controlled and followed the same design as that used in previous studies (Table 1). Groups of immunized and challenged, challenge control, and immunized but not challenged animals were used. Following immunization with one or more exposures of various doses of *O. turkestanicum* cercariae the animals were challenged 9 weeks later with 300 cercariae of *S. bovis*

Table 1. Heterologous immunity in mice exposed to *O. turkestanicum* and challenged with *S. bovis*, *S. haematobium*, and *S. mansoni*

Experiment no.	Cercarial dose: immunizing versus challenge species	Mean adult worm recoveries						Reduction in adult worms (%)	Mean egg counts per g of tissue						Reduction in eggs (%)
		Group A[a]		Group B[a]		Group C[c]			Group A		Group B		Group C		
		O.t.	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*S.b.*
1	100 *O. turkestanicum* versus 300 *S. bovis*	17	—	20	12	—	17	29	800	—	2 200	10 000	—	20 000	50
2	3×50 *O. turkestanicum* versus 300 *S. bovis*	12	—	11	17	—	22	23	600	—	600	13 000	—	29 000	55
3	200 *O. turkestanicum* versus 300 *S. bovis*	49	—	44	12	—	18	33	1 600	—	1 600	10 200	—	21 200	52
		O.t.	*S.h.*	*O.t.*	*S.h.*	*O.t.*	*S.h.*	*S.h.*	*O.t.*	*S.h.*	*O.t.*	*S.h.*	*O.t.*	*S.h.*	*S.h.*
4	3×50 *O. turkestanicum* versus 300 *S. haematobium*	16	—	21	20	—	22	9	900	—	5 200	9 300	—	15 900	42
		O.t.	*S.m.*	*O.t.*	*S.m.*	*O.t.*	*S.m.*	*S.m.*	*O.t.*	*S.m.*	*O.t.*	*S.m.*	*O.t.*	*S.m.*	*S.m.*
5	50 *O. turkestanicum* versus 150 *S. mansoni*	10	—	7	30	—	41	27	—	—	1 000	48 000	—	51 700	7
6	200 *O. turkestanicum* versus 150 *S. mansoni*	48	—	38	33	—	41	20	2 100	—	1 400	32 100	—	51 700	38

[a] Immune control group (immunized but not challenged).
[b] Immunized and challenged group.
[c] Challenge control group (challenged only).

or of *S. haematobium*, or 150 cercariae of *S. mansoni*. The cercariae at each exposure were all taken from the same suspension obtained from a large number of infected snails.

Experiment 1: mice immunized with O. turkestanicum (100 cercariae) and challenged with S. bovis (300 cercariae)

The recoveries of schistosomes showed that the mean worm burden of *S. bovis* in the immunized group was slightly lower than in the challenge control group. The *S. bovis* egg counts in the liver and gut, and total egg counts per mouse, were markedly lower (50%) in the immunized group than in the challenge control group. The differences between the means in the liver, gut, and total egg counts were all statistically significant ($P<0.05$, $P<0.01$, and $P<0.02$, respectively).

Experiment 2: mice immunized with O. turkestanicum (3×50 cercariae) and challenged with S. bovis (300 cercariae)

Immunization was carried out by 3 repeated inoculations of 50 *O. turkestanicum* cercariae at 4-week intervals. The challenge exposure with *S. bovis* cercariae was carried out 4 weeks after the last exposure to *O. turkestanicum* cercariae.

As indicated in Table 1 the mean recovery of *S. bovis* from the challenge infection was again slightly lower in the immunized and challenged group than in the challenge control group. Analysis showed that the liver, gut, and total egg counts per mouse in the immunized and challenged group were 55% lower than in the challenge control group. Student's *t*-test showed that the differences between the means of the eggs in liver and gut and the total eggs of these two groups were significant ($P<0.05$, $P<0.02$, and $P<0.02$ respectively). The total number of eggs per female was markedly lower in the immunized group.

Experiment 3: mice immunized with O. turkestanicum (200 cercariae) and challenged with S. bovis (300 cercariae)

There was a reduction of 33% in worm burdens of *S. bovis* in the immunized group. The liver and total egg counts per mouse showed significant reductions ($P<0.05$ and $P<0.05$), but the gut egg count did not. The number of eggs per female was also higher in the non-immunized group.

Experiment 4: mice immunized with O. turkestanicum (3×50 cercariae) and challenged with S. haematobium (300 cercariae)

Although the reduction in the number of adult *S. haematobium* (9%) was not significant, there was a significant reduction (42%) in the liver egg counts ($P<0.01$) and in total eggs per mouse ($P<0.05$).

Experiment 5: mice immunized with O. turkestanicum (50 cercariae) and challenged with S. mansoni (150 cercariae)

There was a reduction of 27% in the number of *S. mansoni* adults but the tissue egg counts were reduced by only 7%. An interesting observation was the presence of *O. turkestanicum* eggs in the immunized animals although none were found in the control mice infected with *O. turkestanicum*.

Experiment 6: mice immunized with O. turkestanii cum (200 cercariae) and challenged with S. manson- (150 cercariae)

With the increased cercarial dose the mean total tissue egg count showed a 38% reduction in the immunized group. This reduction and the reductions in the liver and gut egg counts were all statistically significant ($P<0.02$, $P<0.05$, and $P<0.05$ respectively). *O. turkestanicum* eggs were seen in both the immunized and control animals.

Comment on experiments in mice

The results show a considerable degree of heterologous immunity with all the systems tested except when a low dose of *O. turkestanicum* was used against challenge with *S. mansoni*. The experiments with *O. turkestanicum* showed that although it reached maturity in mice it usually produced only a few eggs when given alone; in combined infections with *S. bovis* or *S. haematobium*, however, a considerable number of *O. turkestanicum* eggs were found in the tissues. A similar phenomenon of heterospecific stimulation, in which *S. mattheei* responded to the presence of *S. mansoni*, was reported by Taylor et al. (1969).

A single exposure to *O. turkestanicum* cercariae was as effective as multiple exposure in producing immunity. This is in contrast to our previous observations on *S. mattheei* and *S. mansoni* (Amin & Nelson, 1969). Moreover, there was no apparent increase in effectiveness when the immunizing dose was in-

Table 2. Effect of heterologous immunity on recoveries O of adult. *turkestanicum, S. bovis,* and *S. haematobium* in calves and sheep

Experiment no.	Cercarial dose: immunizing versus challenge species	Mean adult worm recoveries						Reduction in adult worms (%)
		Group A[a]		Group B[b]		Group C[c]		
		O.t.	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*S.b.*
7. Calves	8 000 *O. turkestanicum* versus 5 000 *S. bovis*	3 251	—	2 186	1 966	—	3 156	38
		S.b.	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*O.t.*
8. Calves	5 000 *S. bovis* versus 8 000 *O. turkestanicum*	3 530	—	3 210	2 283	—	3 251	30
		S.h.	*S.b.*	*S.h.*	*S.b.*	*S.h.*	*S.b.*	*S.b.*
9. Calves	3×7 000 *S. haematobium* versus 5 000 *S. bovis*	—	—	334	1 819	—	3 156	42
		S.h.	*O.t.*	*S.h.*	*O.t.*	*S.h.*	*O.t.*	*O.t.*
10. Calves	3×7 000 *S. haematobium* versus 8 000 *O. turkestanicum*	—	—	422	2 230	—	3 251	31
		O.t.	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*S.b.*
11. Sheep	5 000 *O. turkestanicum* versus 5 000 *S. bovis*	1 774	—	1 574	1 974	—	2 151	8
		S.b.	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*O.t.*
12. Sheep	5 000 *S. bovis* versus 5 000 *O. turkestanicum*	2 151	—	1 992	1 000	—	1 774	44

[a] Immune control group (immunized but not challenged).
[b] Immunized and challenged group.
[c] Challenge control group (challenged only).

creased from 100 to 200 cercariae. It is possible that with this system there is a minimum effective immunizing level below 100 cercariae similar to the threshold recorded for *S. mansoni* by Smithers & Terry (1965) in rhesus monkeys.

HETEROLOGOUS IMMUNITY STUDIES IN CALVES AND SHEEP

The calves and sheep were divided into groups of 2 or 3 animals. The challenge control group in one experiment served as the control for the other experiments. The immunizing and challenging doses of cercariae consisted of a single exposure of 8 000 cercariae of *O. turkestanicum* or 5 000 *S. bovis* in calves and 5 000 cercariae of *O. turkestanicum* or *S. bovis* in sheep. The calves immunized with *S. haematobium* were given 3 inoculations of 7 000 cercariae in each inoculation at 4-week intervals.

Autopsy was performed 9 weeks after the challenge exposure. The mean worm recoveries (Table 2) and egg counts per gram of tissue (Table 3) were the criteria used to evaluate the degree of resistance.

Experiment 7 : calves immunized with O. turkestanicum (8 000 cercariae) and challenged with S. bovis (5 000 cercariae)

The calves were divided into 3 groups. Group A consisted of 3 calves that were exposed to 8 000 cercariae of *O. turkestanicum* but not challenged; they were killed 9 weeks after exposure. Group B consisted of 3 calves each exposed to 8 000 cercariae of *O. turkestanicum* and challenged 9 weeks later with 5 000 cercariae of *S. bovis*; they were killed after a further 9 weeks. Group C, which served as controls for the calves in group B, consisted of 2 calves each exposed to only 5 000 cercariae of *S. bovis.*

The number of adult *S. bovis* recovered from the immunized calves was 38% lower than that recovered

Table 3. Effect of heterologous immunity on tissue egg densities of *O. turkestanicum*, *S. bovis*, and *S. haematobium* in calves and sheep

Experiment no.	Cercarial dose: immunizing versus challenge species	Tissues examined for eggs	Mean egg counts per g of tissue						Reduction in eggs (%)
			Group A[a]		Group B[b]		Group C[c]		
			O.t.	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*S.b.*
7. Calves	8 000 *O. turkestanicum* versus 5 000 *S. bovis*	liver	404	—	112	872	—	3 076	71.7
		small intestine	17 567	—	10 300	735	—	2 138	65.6
		large intestine	0	—	0	1 123	—	4 721	76.2
			S.b.	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*O.t.*
8. Calves	5 000 *S. bovis* versus 8 000 *O. turkestanicum*	liver	3 076	—	2 133	156	—	404	61.4
		small intestine	2 138	—	1 266	4 001	—	17 567	77.2
		large intestine	4 721	—	943	0	—	0	—
			S.h.	*S.b.*	*S.h.*	*S.b.*	*S.h.*	*S.b.*	*S.b.*
9. Calves	21 000 *S. haematobium* versus 5 000 *S. bovis*	liver	—	—	0	2 150	—	3 076	30.1
		small intestine	—	—	0	1 175	—	2 138	45.0
		large intestine	—	—	0	430	—	4 721	90.9
			S.h.	*O.t.*	*S.h.*	*O.t.*	*S.h.*	*O.t.*	*O.t.*
10. Calves	21 000 *S. haematobium* versus 8 000 *O. turkestanicum*	liver	—	—	8	333	—	404	17.6
		small intestine	—	—	16	3 019	—	17 567	82.8
		large intestine	—	—	20	0	—	0	—
			O.t.	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*S.b.*
11. Sheep	5 000 *O. turkestanicum* versus 5 000 *S. bovis*	liver	1 095	—	723	7 815	—	9 757	19.9
		small intestine	8 880	—	6 950	3 919	—	4 635	15.4
		large intestine	0	—	0	3 684	—	5 005	26.4
			S.b.	*O.t.*	*S.b.*	*O.t.*	*S.b.*	*O.t.*	*O.t.*
12. Sheep	5 000 *S. bovis* versus 5 000 *O. turkestanicum*	liver	9 757	—	24 073	138	—	1 095	87.4
		small intestine	4 635	—	14 752	6 912	—	8 880	22.2
		large intestine	5 005	—	8 215	0	—	0	—

[a] Immune control group (immunized but not challenged).
[b] Immunized and challenged group.
[c] Challenge control group (challenged only).

from the challenge control group. There were reductions in tissue egg counts of 72%, 66%, and 76% in the liver, small intestine, and larger intestine, respectively.

Experiment 8: calves immunized with S. bovis (5 000 cercariae) and challenged with O. turkestanicum (8 000 cercariae)

The design of this study was similar to that of the previous experiment, except that there were 3 animals in groups B and C while group A had 2 animals. The number of immunizing *S. bovis* cercariae was 5 000, challenged by 8 000 cercariae of *O. turkestanicum*.

The mean number of *O. turkestanicum* adults in group B was 30% lower than that in group C. The reductions in tissue egg counts per gram of liver and small intestine were 61% and 77%, respectively.

Experiment 9: calves immunized with S. haematobium (3×7 000 cercariae) and challenged with S. bovis (5 000 cercariae)

Calves in group B were immunized with 3 doses of 7 000 *S. haematobium* cercariae at 4-week intervals, making a total of 21 000 cercariae per calf. The challenge was the same as in experiment 7.

The mean recovery of *S. bovis* worms in group B was 42% below that in group C. Distinguishing *S. haematobium* from *S. bovis* was relatively easy, since the *S. haematobium* worms were almost all very small and immature with undeveloped internal organs, but there may have been some errors owing to the stunting effect of the immunity on *S. bovis*. The *S. bovis* egg counts in the liver, small intestine, and large intestine were all reduced in the immunized animals (by 30%, 45%, and 91%, respectively.)

Experiment 10: calves immunized with S. haematobium (3×7 000 cercariae) and challenged with O. turkestanicum (8 000 cercariae)

The mean recovery of adult *O. turkestanicum* was 31% lower in group B than in group C. The corresponding reduction in tissue egg counts was 17% in the liver and 82% in the small intestine.

Experiment 11: sheep immunized with O. turkestanicum (5 000 cercariae) and challenged with S. bovis (4 000 cercariae)

The sheep proved to be highly susceptible to both parasites. The reduction in the *S. bovis* worm burden in group B was 8%. Tissue egg counts were reduced by 20% in the liver, 15% in the small intestine, and 26% in the large intestine.

Experiment 12: sheep immunized with S. bovis (5 000 cercariae) and challenged with O. turkestanicum (5 000 cercariae)

In the reverse experiment the immune effect was more impressive, with a reduction of 44% in adult *O. turkestanicum* and a reduction in tissue egg counts of 87% in the liver and 22% in the small intestine. However, these experiments should be repeated because of the extreme variation between the 2 immunized animals; in one the total number of adult *O. turkestanicum* recovered was 432, with no eggs in the liver and a very low egg count of 350 eggs per gram of small intestine, whereas the other sheep in group B had 1 569 worms and 13 475 eggs per gram of small intestine.

Comment on experiments in calves and sheep

Detailed accounts of the pathology of *O. turkestanicum* and *S. bovis* in naturally infected and experimentally infected cattle, sheep, and goats will be published elsewhere (Massoud, unpublished data). A striking difference between these 2 parasites is the marked localization of *O. turkestanicum* adults in the upper mesenteric veins; most of the eggs are found in the duodenum, with very few in the liver and none in the large intestine. On the other hand, *S. bovis* and *S. mattheei* worms are distributed widely throughout the large and small bowel and the liver is often seriously affected. *O. turkestanicum* is therefore much less pathogenic than these other bovine schistosomes. It is of considerable interest that the calves exposed to this relatively benign parasite developed a marked resistance to challenge with *S. bovis* at cercarial densities that would normally have seriously affected them.

The results with *S. haematobium* were even more striking as this parasite is generally regarded as being noninfective to livestock. Exposure of the calves to large doses of *S. haematobium* showed that a considerable number of worms develop to the adult stage. In the 4 animals exposed to 21 000 cercariae the worm recovery rates were 640 (3%), 204 (0.9%), 418 (1.9%), and 250 (1.2%). Only in the first animal were eggs recovered, the counts being 16 per g in the liver, 33 per g in the small intestine, and 40 per g in the large intestine. The eggs were all deformed and blackened and contained no miracidia. These animals were infected with both *S. haematobium* and *O. turkestanicum*, so this may be another example of heterospecific stimulation. The report by McKenzie (1970) of finding natural infections of *S. haematobium* and *S. mansoni* in sheep in Southern Rhodesia may have a similar explanation although in Southern Rhodesia there is a possibility of confusion with small eggs of *S. mattheei*, which would be difficult to distinguish from *S. haematobium*.

The most effective heterologous immunity was developed by the cattle given 3 exposures to *S. haematobium* and challenged with *O. turkestanicum*. There was also good cross protection against *S. bovis*, which again showed that a nonpathogenic schistosome can give considerable protection against infection with a pathogenic form. Hsu et al. (1966) had some success with the reverse experiment in protecting rhesus monkeys against *S. haematobium* by repeated immunization with an Iranian strain of *S. bovis*.

The results of the experiments in sheep were less dramatic but again some protection was demonstrated.

SUPPLEMENTARY HOMOLOGOUS IMMUNITY EXPERIMENTS IN MICE AND CALVES

The main purpose of this series of studies has been to observe the interaction of different species of animal and human schistosomes. As there was abundant material available in Iran, however, the opportunity was taken to study the effect of homologous immunity to *S. bovis* and to *O. turkestanicum* (see Table 4).

Experiment 13: mice immunized with S. bovis (100 cercariae) and challenged with S. bovis (300 cercariae)

The experiment followed the same pattern as experiments 1–6. A marked immunity developed,

Table 4. Homologous immunity to *S. bovis* in mice and to *O. turkestanicum* and *S. bovis* in calves

Experiment no.	Cercarial dose: immunization versus challenge	Mean adult worm recoveries			Reduction in adult worms (%)	Tissues examined for eggs	Mean egg counts per g of tissue			Reduction in eggs (%)
		Group A[a]	Group B[b]	Group C[c]			Group A	Group B	Group C	
13. Mice	100 *S. bovis* versus 300 *S. bovis*	7	12	34	65	whole mouse	7 000	29 000	57 000	49.0
14. Calves	1 000 *S. bovis* versus 4 000 *S. bovis*	—	3 242	2 893	0	liver	—	1 168	1 438	18.8
						small intestine	—	1 832	3 453	46.9
						large intestine	—	508	2 116	76.0
15. Calves	1 000 *O. turkestanicum* versus 4 000 *O. turkestanicum*	—	1 400	2 434	42	liver	—	113	110	0
						small intestine	—	3 260	12 000	72.8
						large intestine	—	—	—	—

[a] Immune control group (immunized but not challenged).
[b] Immunized and challenged group.
[c] Challenge control group (challenged only).

with a 66% reduction in the adult *S. bovis* burden ($P<0.001$) and a reduction of 49% in total eggs per mouse. The P values for the differences in the egg counts in the liver and gut and in total egg counts per mouse were $P<0.2$, $P<0.02$, and $P<0.05$, respectively.

Experiment 14: calves immunized with S. bovis (1 000 cercariae) and challenged with S. bovis (4 000 cercariae)

Calves were divided into immunized and non-immunized groups. There was no significant difference in the number of adult worms recovered from the immunized and control animals; in fact there were more in the immunized group—3 200 against 2 900. The tissue egg counts were reduced in the immunized animals by 19% in the liver, 47% in the small intestine, and 76% in the large intestine.

Experiment 15: calves immunized with O. turkestanicum (1 000 cercariae) and challenged with O. turkestanicum (4 000 cercariae)

The mean number of *O. turkestanicum* adults recovered in the immunized group was 1 400 compared with 2 434 in the control group, a reduction of 42%. The immunity had no effect on the egg densities in the liver but there was a reduction of 73% in the egg counts from the small intestine.

Comment on experiments 13–15

The experiment with *S. bovis* in mice showed that this system could be used for studying homologous immunity. This is in contrast to the system of *S. mansoni* in mice, which has given disappointing results in homologous immunity studies (Smithers, 1962).

The demonstration of a well-developed homologous immunity in cattle against both *S. bovis* and *O. turkestanicum* is of interest not only in relation to its possible significance in the field but also because of the potential value of the model for studying immunity in a normal host–parasite system. All previous studies on homologous immunity in schistosomiasis have been of artificial systems, usually *S. mansoni* in mice, rhesus monkeys, or rats, and there has been a tendency to assume that the findings are of direct relevance to immunity in schistosomiasis in man or domestic animals.

DISCUSSION

The results of these experiments with *O. turkestanicum*, *S. bovis*, *S. mansoni*, and *S. haematobium* confirm our earlier observations that there is considerable cross resistance between different species of schistosome (Amin et al., 1968; Nelson et al., 1968; Amin & Nelson, 1969; Hussein et al., 1970; Preston et al., 1972). The accumulated evidence suggests that previous exposure to animal schistosomes may be of significance in protecting man from the more serious effects of *S. mansoni*, *S. haematobium*, or *S. japonicum* infections. This phenomenon, which is of considerable importance in many infectious diseases, has been named " zooprophylaxis " and is defined as " the prevention or amelioration of disease in man as a result of previous exposure to natural infections of animal origin " (Nelson et al., 1962). The experiments described here and those

reported by Hussein et al. (1970) and Preston et al. (1972) on *S. mansoni* versus *S. mattheei* in calves and sheep clearly demonstrate that the reverse type of heterologous immunity may be of considerable importance in protecting cattle and sheep from the more serious effects of animal schistosomiasis. The heterologous responses occur not only between human and animal parasites, e.g., *S. haematobium* and *S. bovis*, but also between different species of animal schistosome, e.g., *O. turkestanicum* and *S. bovis*.

There is increasing evidence that schistosomiasis can be a serious economic problem in the livestock industry. *S. mattheei* is widespread in southern Africa, causing severe outbreaks in cattle and sheep (Le Roux, 1929; Condy, 1960; Strydom, 1963; Hurter & Potgieter, 1967; Lawrence, 1968; McCully & Kruger, 1969; Reinecke, 1970; Lawrence & Condy, 1970). In Central and North Africa *S. mattheei* is replaced by *S. bovis*; serious consequences of this disease have been reported from cattle in East Africa (Dinnik & Dinnik, 1965) and the Sudan (Malek, 1969; Hussein, 1971).[1] It is also a problem in Corsica (Brumpt, 1930), Sardinia (Coluzzi et al., 1965), Israel (Lengy, 1962), Iraq (McHattie & Chadwick, 1932), and Iran (Arfaa et al., 1965; Massoud, unpublished data). Other species of schistosome that are of importance in the livestock industry include *S. japonicum*, *S. spindale*, *S. nasalis*, *S. incognitum*, *Ornithobilharzia bomfordi*, and *O. turkestanicum* (see, for example, Lapage, 1962).

The problem of schistosomiasis in livestock is probably greatly underestimated as most studies have been carried out on animals slaughtered in abattoirs. In many areas only the relatively fit animals—those that have developed some degree of immunity—are accepted for slaughter. It may therefore be that many young animals die of the infection and that older animals seriously affected by the disease fail to reach the abattoirs. This is certainly true of animals living in the epizootic conditions reported from South Africa and the Sudan. There is an obvious need to reassess the economic significance of schistosomiasis in livestock and to evaluate the role of immunity in limiting the severity of the disease.

Our experiments on the interaction of schistosomes suggest that the simultaneous transmission of *S. bovis* and *S. haematobium* in the same area may be to the mutual benefit of man and his livestock in reducing the effects of schistosomiasis. In Iran *S. haematobium* and *S. bovis* are transmitted by the same intermediate snail host and the campaign to limit the human disease by the application of molluscicides has resulted in a simultaneous decrease in the infection rates in cattle and man (Massoud & Nelson, 1972). It may therefore be too late to assess the significance of heterologous immunity between *S. haematobium* and *S. bovis* in this particular area. However, there are many other areas in the Middle East and Africa where field studies could be carried out on the interaction of different species of schistosome. Further studies are also necessary to develop optimum immunization procedures in cattle and sheep with a view to field trials to test the efficacy of heterologous immunity in areas where schistosomiasis is an important veterinary problem. In previous studies (Hussein et al., 1970; Preston et al., 1972) we found that *S. mansoni* was a useful immunizing agent against *S. mattheei* in cattle and sheep, but a few of the animals produced patent *S. mansoni* infections that might potentiate its transmission to man in areas where *Biomphalaria* snails are prevalent. The present studies confirm the previous observations of Kuntz & Malakatis (1955) with goats, McHattie et al. (1933) and Saeed [2] with sheep, and Saoud (1966) with pigs that *S. haematobium* is unlikely to produce viable eggs in livestock. Sufficient adult worms develop in cattle to stimulate immunity without causing pathological effects and without producing viable eggs. This parasite could therefore be used as an innocuous immunizing agent with very little risk of transmission to man.

[1] See also Hussein, M. F. (1969) *The pathology of spontaneous and experimental bovine schistosomiasis. A study of the spontaneous disease and of experimental infestations of calves and mice with* Schistosoma bovis *and* Schistosoma mattheei, Ph. D. Thesis, University of London.

[2] Saeed, A. A. (1970) *Observations on the pathogenesis of schistosomiasis in mice, calves and sheep*, Ph. D. Thesis, University of London.

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RÉSUMÉ

ÉTUDE DE L'IMMUNITÉ HÉTÉROLOGUE DANS LA SCHISTOSOMIASE: 6. OBSERVATIONS SUR L'IMMUNITÉ CROISÉE ENVERS *ORNITHOBILHARZIA TURKESTANICUM*, *SCHISTOSOMA BOVIS*, *S. MANSONI* ET *S. HAEMATOBIUM* CHEZ DES SOURIS, DES MOUTONS ET DES BOVINS EN IRAN

De précédentes études ont montré qu'un degré notable d'immunité protectrice hétérologue apparaît chez des souris, des singes et des bovins infectés par diverses espèces de schistosomes d'origine humaine ou animale. Des recherches similaires ont été faites chez des souris, des bovins et des moutons exposés à l'infection par des schistosomes fréquemment rencontrés en Iran.

L'infection de souris par *Ornithobilharzia turkestanicum* leur confère une protection élevée contre une infection d'épreuve par *Schistosoma bovis*, *S. haematobium* et *S. mansoni*. Chez les animaux exposés au préalable à 100-200 cercaires d'*O. turkestanicum*, puis à 300 cercaires de *S. bovis*, 300 cercaires de *S. haematobium* ou 150 cercaires de *S. mansoni*, on note une réduction de la charge parasitaire de 23-33% pour *S. bovis*, 9% pour *S. haematobium* et 20-27% pour *S. mansoni*, tandis que le nombre d'œufs présents dans les tissus est réduit de 50-56%, 42%, et 7-38% respectivement.

Chez les bovins, des résultats plus concluants encore ont été obtenus. Après immunisation par exposition à 21 000 cercaires de *S. haematobium*, suivie d'une infection d'épreuve par 5 000 cercaires de *S. bovis*, le nombre d'adultes de ce dernier schistosome est réduit de 42%, le nombre d'œufs présents dans le foie de 30% et celui des œufs décelés dans le gros intestin de 91%. Une immunité croisée du même ordre se manifeste en cas d'immunisation suivie d'infection d'épreuve par *O. turkestanicum* et *S. bovis* d'une part, *S. bovis* et *O. turkestanicum* d'autre part, enfin *S. haematobium* et *O. turkestanicum*. L'immunisation de moutons par *O. turkestanicum* leur confère une protection de moindre niveau contre l'infection par *S. bovis*, mais de bons résultats sont observés lorsqu'on inverse l'ordre d'exposition aux schistosomes.

D'autre part, lorsque des souris exposées à 100 cercaires de *S. bovis* sont soumises ensuite à une infection d'épreuve par 300 cercaires du même parasite, la charge parasitaire en adultes est réduite de 65% et le nombre d'œufs présents dans les tissus de 49%. Chez des bovins exposés successivement à 1 000 cercaires puis à 4 000 cercaires de *S. bovis*, le nombre de vers adultes n'est pas diminué mais la quantité d'œufs est réduite de 19% dans le foie et de 76% dans l'intestin.

Les auteurs pensent qu'il serait intéressant de procéder à des essais sur le terrain pour voir s'il est possible, en mettant à profit l'immunité hétérologue, d'atténuer la gravité de la schistosomiase dans le bétail. Ainsi *S. haematobium*, qui parvient à maturité chez le bétail sans produire d'œufs viables, pourrait conférer une protection contre *S. bovis*.

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