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Immunological Responses of the Mammalian Host against Tapeworm Infections

IV. SPECIES SPECIFICITY OF HEXACANTH EMBRYOS IN PROTECTING SHEEP AGAINST *ECHINOCOCCUS GRANULOSUS*

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Summary. Eighty lambs were divided into four groups, each comprising twenty animals. Half the lambs in each group were vaccinated with viable eggs and half with the activated embryos of *Echinococcus granulosus*, *Taenia hydatigena*, *T. ovis* or *T. pisiformis*. These lambs together with ten control animals were subsequently challenged with eggs of *E. granulosus*.

Only a few hydatid cysts were established from the challenge infection in the lambs immunized with the homologous eggs or embryos. Only one acephalocyst in one animal survived. The metabolism of this cyst was of a low order compared with that of most of those in the controls.

Hydatid cysts were established from the challenge infection almost as frequently in the animals vaccinated with eggs or embryos of the sheep metacestodes *T. hydatigena* and *T. ovis*, as in the controls. Fluid accumulated in only a few hydatid cysts from the challenge infection in those sheep vaccinated with the activated embryos of these heterologous species.

The injection of viable eggs or activated embryos of the rabbit metacestode *T. pisiformis* induced no resistance to the establishment or to the survival of the challenge infection of *E. granulosus*.

INTRODUCTION

Three previous studies (Gemmell, 1964, 1965a, b) using *Taenia hydatigena*, *T. ovis* in sheep and *T. pisiformis* as the test challenge organism in rabbits, demonstrated that a relatively solid resistance to both the establishment and to the long-term survival of each species is induced by a prior intramuscular injection of the homologous viable eggs or the activated embryos.

The cross-protection studies showed that immunity to *T. hydatigena* and to *T. ovis*, in sheep, is induced by vaccination with the activated embryos of the heterologous species. No protection against these two sheep metacestodes is induced by vaccination with the activated embryos or eggs of the rabbit metacestode *T. pisiformis*. Similarly no effective protection is induced to *T. pisiformis* in rabbits by vaccination with the eggs or activated embryos of these sheep metacestodes.

These three previous studies have been made on tapeworms of the same genus. The present study extends these results by examining the cross-immunity between species of different genera by comparing the ability of the immunogenic complexes of the viable eggs and activated embryos of *Echinococcus granulosus* (homologous), *T. hydatigena* (heterologous), *T. ovis* (heterologous) and *T. pisiformis* (heterologous) to induce a resistance to the establishment and subsequent survival of a challenge infection of *E. granulosus* in sheep. With the exception of *T. pisiformis*, sheep are normal intermediate hosts for these species. *E. granulosus* is one of the aetiological agents of hydatid disease in men.

MATERIALS AND METHODS

Lambs were removed from their dams within 48 hours of birth and raised in a worm-free (*Strongyloides* spp. excepted) environment on cow's milk, concentrates, sterilized hay, vitamin and mineral supplements. One year after the challenge infection had been given and until autopsy, the animals were placed on pasture.

Eggs were expressed from gravid segments of tapeworms collected from dogs infected in the field or in the laboratory, and were stored in water at 6° for up to 14 days before use.

Preparation of vaccines

The method of preparation of each of the antigens used in these trials has been described (Gemmel, 1964). Each dose of antigen of *T. hydatigena* and *T. ovis* (but not *E. granulosus* or *T. pisiformis*) to be injected as activated embryos was placed in a pepsin solution for 40 minutes at 37°. These, and those of *E. granulosus* and *T. pisiformis* were then placed in artificial digestion solution (Silverman, 1954) for up to 20 minutes at 37°. Each batch of eggs was immersed in Silverman's solution for the previously determined period which gave the maximum activity and, at the same time, avoided excessive digestion of the activating embryos. Silverman's solution was then replaced by fresh rabbit serum for the embryos of *T. pisiformis*, and fresh lambs' serum for the embryos of the three sheep metacestodes. Approximately 1 ml of serum at 37°, containing the activated embryos, was injected into the left thigh muscles. Viable eggs were also injected in lambs' or rabbits' serum. The control lambs were injected with both lambs' and rabbits' serum.

Design of experiment

A total of ninety lambs was used in this experiment. Ten were vaccinated with viable eggs and ten with activated embryos of *E. granulosus*, *T. ovis*, *T. hydatigena* and *T. pisiformis*. The ten animals in each sub-group were further divided into five groups of two lambs, which were injected with 1000, 2000, 5000, 20,000 and 50,000 eggs or activated embryos respectively. Ten lambs were used as controls.

The bulk batches of eggs making up each vaccine were tested for contamination with other species of tapeworms by feeding previously unexposed animals with an oral infection with eggs from each batch.

The lambs were vaccinated between 40 and 70 days of age and challenged 94 days later with an aliquot portion containing 2500 fresh eggs of *E. granulosus*, given by intraruminal injection. The interval between challenge and post-mortem examination was 30 ± 1 months. The challenge dose of eggs of *E. granulosus* was given by intraruminal injection.

At autopsy, the abdominal viscera were examined. Twenty-four hours later the heart, liver, lungs, diaphragm, kidneys and the whole skeletal musculature of each animal were examined in detail for hydatid cysts by thinly slicing all tissues at intervals not greater than 0·25 cm. Fluid was withdrawn from each cyst and measured. The diameter of each cyst was also measured. The viability of each cyst was determined by the presence of a cyst germinal membrane and the amount of fluid or solid material present.

Two phases of resistance to infection can be determined. The first phase is the number of hydatid cysts which are established by feeding a known number of eggs. The second phase is concerned with the number of cysts which survive and accumulate fluid. Resistance developed to each phase by each treatment has been assessed in this study, by counting the number of viable and dead cysts in each vaccinated sheep and comparing these numbers with those found in the untreated (control) sheep also fed a similar number of eggs.

Fourteen of the ninety sheep failed to survive the 30-month trial period. These were autopsied at death, but are excluded from the analysis, since survival rates have been determined at about 30 months after ingestion of eggs.

RESULTS

VARIATION IN THE RATE OF INFECTION WITH *E. granulosus* IN PREVIOUSLY UNEXPOSED SHEEP

In this trial, all ten previously unexposed sheep (controls) fed 2500 eggs by intraruminal injection were susceptible to the establishment of an infection with *E. granulosus*. A mean value of 40·5 per cent (range 0·6–100 per cent) of the hydatid cysts established, survived for 30 months (Table 1).

TABLE 1

VARIATION IN THE NUMBER OF HYDATID CYSTS ESTABLISHED AND SURVIVING FOR 30 MONTHS IN PREVIOUSLY UNEXPOSED SHEEP (CONTROLS) FED WITH 2500 EGGS OF *Echinococcus granulosus*

Sheep No.	Site of election					
	Liver			Lungs		
	Total viable retarded and necrotic	Viable	% viable	Total viable retarded and necrotic	Viable	% viable
1497	77	0	0·0	77	1	1·3
650	88	7	8·0	20	9	45·0
1129	60	60	100·0	40	40	100·0
647	27	0	0·0	37	37	100·0
1499	48	0	0·0	6	2	33·3
649	39	38	97·4	11	11	100·0
1496	22	0	0·0	26	26	100·0
646	13	3	23·1	17	7	41·2
648	15	9	60·0	4	4	100·0
1131*		Died				
Total	389	117	30·1	238	137	57·3

* Sheep 1131 died 5 months after feeding with eggs; 314 lesions were observed, of which 165 were in the liver and the remainder in the lungs. Fluid was observed in 122 cysts and the diameter of them exceeded 2·5 mm.

Dead cysts were recognized at 30 months by a zone of cells associated with chronic inflammatory changes and fibrous tissue, and a core of necrotic material. In some cases no inner core of necrotic tissue was present and the germinal layer could not be distinguished. In these, the cavity of no more than a few millimetres, contained little or no fluid and was acephalocystic. It could not be determined whether or not these cysts were dead or latent. Lesions of this type have been recorded as retarded, but in the analysis have been regarded as moribund and included with those which were obviously dead.

Growth, fluid volume and pleomorphic characteristics of hydatid cysts varied considerably in the same animal. The variation in these characters in the untreated (control) sheep fed 2500 eggs is summarized in Table 5. Protoscolices were present in some cysts with a volume of less than 4 ml and in almost all cysts exceeding this volume. The maximum volume, observed in one cyst, was 51 ml. More hydatid cysts were observed in the liver than in the lungs, but this may be due to the difficulties in detecting small lesions* in pulmonary tissue at autopsy compared to the liver. The proportion of viable cysts was greater in the lung than the liver.

Hydatid cysts were of two types, unilocular and bilocular or multilocular. Bi- and multilocular forms differentiated early and were observed in sheep that died within a few months of the challenge infection. The unilocular hydatid cysts were viable more frequently than the bi- and multilocular forms.

VARIATION IN THE RATE OF INFECTION FROM THE INTRAMUSCULAR INJECTION OF THE EGGS AND ACTIVATED EMBRYOS OF *E. granulosus*, *T. hydatigena*, *T. ovis* AND *T. pisiformis*

A few cysts developed at the site of injection or in the adjacent lymph node in some sheep vaccinated with viable eggs or embryos of each sheep metacestode. No cysticerci of *T. pisiformis* were established (Table 2). Only one cysticercus of *T. hydatigena* and none of those of *T. ovis* survived in the muscles for the 30-month period. A hydatid cyst was found

TABLE 2

VARIATION IN THE NUMBER OF CYSTS ESTABLISHED IN THE MUSCLES OF SHEEP FROM AN INTRAMUSCULAR INJECTION OF EGGS OR ACTIVATED EMBRYOS OF *Echinococcus granulosus*, *Taenia hydatigena*, *T. ovis* AND *T. pisiformis*

Parasite	Antigen	No. of sheep surviving for 30 months	No. of cysts established	Variation in No. of cysts established in each animal
E. granulosus	Activated embryos	9	17	0–6
	Viable eggs	8	28	0–14
T. hydatigena	Activated embryos	8	5	0–3
	Viable eggs	8	9	0–4
T. ovis	Activated embryos	9	13	0–5
	Viable eggs	7	3	0–3
T. pisiformis	Activated embryos	10	0	0
	Viable eggs	8	0	0

with 5 ml of fluid in the lymph node draining the site of injection in one sheep immunized with activated embryos of *E. granulosus*. It seems likely that this hydatid cyst developed from the vaccination procedure, rather than from the subsequent intraruminal challenge infection, since cysts of the other two sheep metacestodes also showed some development at the site of injection. In addition, no hydatid cysts developed in the muscles or lymph nodes of the leg in the unvaccinated (control) sheep following feeding with 2500 eggs of *E. granulosus*.

* The large number of hydatid lesions found at autopsy in sheep 1131 at 5 months compared to that in the survivors suggests that some abortive lesions may have been resolved in those autopsied 30 months after challenge. The percentage survival rate, therefore, may be lower than recorded.

TABLE 3

VARIATION IN THE NUMBER OF CYSTS ESTABLISHED AND SURVIVING FROM A CHALLENGE WITH 2500 EGGS OF *Echinococcus granulosus* IN SHEEP VACCINATED WITH HOMOLOGOUS AND HETEROLOGOUS VIABLE EGGS OR ACTIVATED EMBRYOS

Parasite	Antigen	No. of animals*			Average No. necrotic† lesions per animal	Average No. of viable cysts per animal	Average No. of necrotic† lesions and viable cysts per animal
		Uninfected with viable cysts	Infected with 1–10 viable cysts	More than 10 viable cysts			
E. granulosus	Activated embryos	8	1	0	6·0	0·1	6·1
	Viable eggs	8	0	0	5·6	0·0	5·6
T. hydatigena	Activated embryos	5	3	0	45·8	2·1	47·9
	Viable eggs	2	1	5	50·1	30·4	80·5
T. ovis	Activated embryos	7	2	0	42·2	0·4	42·6
	Viable eggs	0	1	6	22·0	33·9	55·9
T. pisiformis	Activated embryos	3	2	5	50·2	24·4	74·6
	Viable eggs	1	1	6	44·0	32·5	75·5
Controls (See Table 1)		0	3	6	41·5	28·2	69·7

* Surviving full term of experiment.
† Necrotic lesions and retarded cysts included together as necrotic.

RESISTANCE TO *E. granulosus* BY SHEEP VACCINATED WITH HOMOLOGOUS AND HETEROLOGOUS VIABLE EGGS AND ACTIVATED EMBRYOS

Homologous antigens

Table 3 summarizes the results. Only two of the seventeen surviving lambs immunized with the homologous viable eggs or activated embryos resisted the establishment of hydatid cysts, but sixteen (94·0 per cent) of these lambs resisted the long-term survival of the challenge injection of *E. granulosus*. Only one viable cyst containing 1·5 ml of fluid but with no protoscolices, was present in the lung of one animal. It is clear that the metabolism of the non-fertile cyst in this animal was of a low order compared to that found in many of the control animals.

Heterologous antigens

Only one of the seventeen surviving animals vaccinated with the activated embryos of *T. hydratigena* or *T. ovis* resisted the establishment of the challenge infection, but in twelve (70·6 per cent) hydatid cysts failed to survive or were grossly retarded. In each of the remainder, less than ten cysts were present, but in three of them at least one cyst contained more than 5 ml fluid. In those surviving sheep vaccinated with the eggs of these two sheep metacestodes, as well as those vaccinated with the activated embryos or eggs of *T. pisiformis*, cyst numbers or growth did not differ significantly from that in the control animals.

VARIATION IN THE DISTRIBUTION OF *E. granulosus* IN SHEEP VACCINATED WITH HOMOLOGOUS OR HETEROLOGOUS EGGS OR ACTIVATED EMBRYOS

Table 4 shows the distribution of hydatid cysts of the challenge infection of *E. granulosus* in each vaccinated group. There was a variation in the proportion of cysts affecting and surviving in the lungs and livers of different animals between groups. As was observed in the control group, the proportion of viable pulmonary cysts was greater than that of viable hepatic cysts in most groups in which vaccination had induced no immunity. This suggests

TABLE 4

DISTRIBUTION OF HYDATID CYSTS FROM A CHALLENGE INFECTION WITH 2500 EGGS OF *Echinococcus granulosus* IN SHEEP VACCINATED WITH HOMOLOGOUS AND HETEROLOGOUS EMBRYOS

Parasite	Antigen	Site of election							
		Liver				Lungs			
		Viable		Retarded or necrotic		Viable		Retarded or necrotic	
E. granulosus	Activated embryos (9)*	0†	(0·0)	34	(61·8)	1	(1·8)	20	(36·4)
	Viable eggs (8)	0	(0·0)	22	(48·9)	0	(0·0)	23	(51·1)
T. hydatigena	Activated embryos (8)	9	(2·3)	223	(58·2)	8	(2·2)	143	(37·3)
	Viable eggs (8)	51	(7·9)	194	(30·1)	192	(29·8)	207	(32·2)
T. ovis	Activated embryos (9)	0	(0·0)	100	(26·0)	4	(1·1)	280	(72·9)
	Viable eggs (7)	37	(9·5)	113	(28·9)	200	(51·1)	41	(10·5)
T. pisiformis	Activated embryos (10)	132	(17·7)	240	(32·2)	112	(15·0)	262	(35·1)
	Viable eggs (8)	53	(8·8)	152	(25·1)	207	(34·3)	192	(31·8)

* The figure in parentheses is the number of animals surviving for 30 months after challenge.
† The first figure is the actual number of cysts, and the figure in parentheses is the percentage of the total number of cysts recovered.

TABLE 5

GROWTH CHARACTERISTICS OF HYDATID CYSTS 30 MONTHS AFTER A CHALLENGE INFECTION WITH 2500 EGGS OF *Echinococcus granulosus* IN SHEEP VACCINATED WITH EGGS OR ACTIVATED EMBRYOS OF *E. granulosus* OR ACTIVATED EMBRYOS OF *Taenia hydatigena* OR *T. ovis* COMPARED WITH UNTREATED SHEEP (CONTROLS) FED 2500 EGGS OF *E. granulosus*

Parasite			Unilocular cysts							Bi- and multilocular cysts						
			Viable			Retarded	Necrotic	Total		Viable			Retarded	Necrotic	Total	
			1–4 ml†	5–9 ml†	>9 ml†	<1 ml†	—	No.	% viable	1–4 ml†	5–9 ml†	>9 ml†	<1 ml†	—	No.	% viable
E. granulosus	Activated	a	0	0	0	0	23	23	0·0	0	0	0	0	11	11	0·0
(9)*	embryos	b	1	0	0	7	5	13	7·7	0	0	0	0	8	8	0·0
E. granulosus	Viable	a	0	0	0	2	13	15	0·0	0	0	0	0	7	7	0·0
(8)	eggs	b	0	0	0	2	3	5	0·0	0	0	0	0	18	18	0·0
T. hydatigena	Activated	a	1	2	5	3	52	63	12·7	1	0	0	22	146	169	0·6
(8)	embryos	b	8	0	0	10	50	68	10·2	0	0	0	40	43	83	0·0
T. ovis	Activated	a	0	0	0	43	37	80	0·0	0	0	0	0	20	20	0·0
(9)	embryos	b	2	0	2	12	226	242	1·7	0	0	0	2	40	42	0·0
Controls	—	a	53	37	26	52	31	199	58·3	1	0	0	30	109	190	0·5
(9)	—	b	38	28	3	14	13	146	81·5	17	1	0	3	71	93	19·4

a, No. of cysts in liver; b, No. of cysts in lung.

* The figure in parentheses is the number of animals surviving for 30 months after challenge.

† Fluid volume.

that the lung may be a slightly more favourable site for the survival of hydatid cysts than the liver. In those groups in which vaccination had induced some immunity (Table 5), both unilocular and multilocular forms were present. All bi- and multilocular forms were dead in sheep vaccinated with the homologous eggs or embryos. Few unilocular forms grew normally in sheep immunized with the activated embryos of *T. hydatigena* and *T. ovis* compared with the number in the control group, but only one multilocular cyst was not grossly retarded or dead. This cyst in a sheep vaccinated with the activated embryos of *T. hydatigena* contained only 1·5 ml of fluid and no protoscolices were present.

COMPARATIVE VALUE OF EACH ANTIGEN COMPLEX IN PROTECTING SHEEP AGAINST *E. granulosus*

Figs. 1 and 2 show the percentage cumulative frequency of animals in the different sub-groups having no more than the specified number of cysts. Fig. 1 (for total lesions) indicates that immunization with the homologous embryos and eggs differs from that with other antigens. A minor effect is observed with the activated embryos of *T. hydatigena* and *T. ovis*. The eggs of these species and the activated embryos and eggs of *T. pisiformis* form similar lines to that for the control group, and, therefore, appear to give no protection against the establishment of the challenge infection of *E. granulosus*.

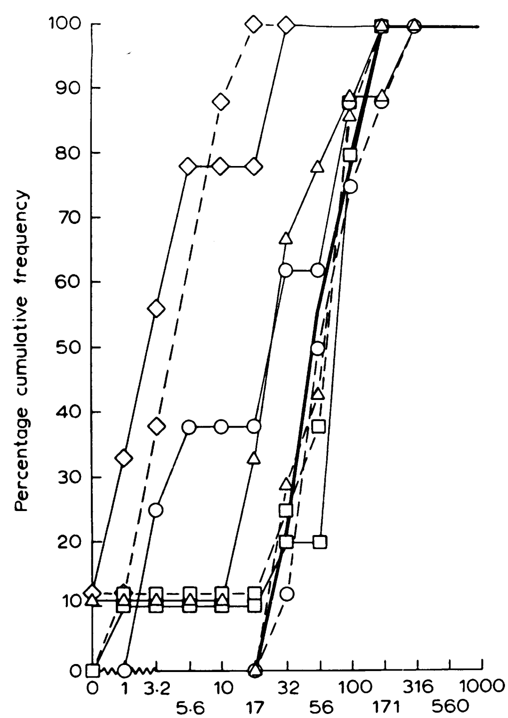

Fig. 1

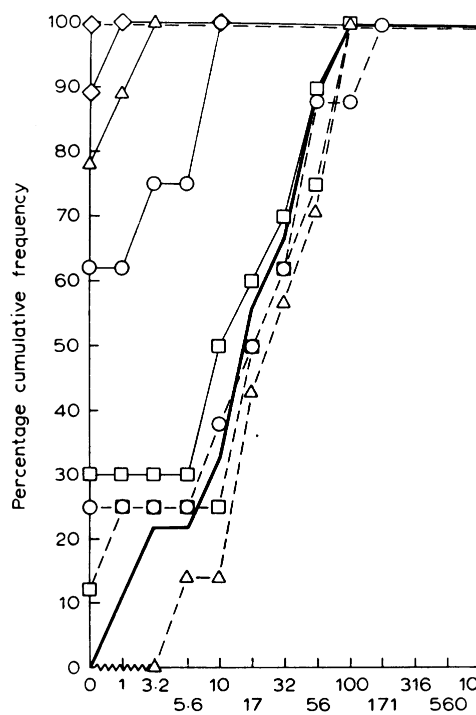

Fig. 2

Figs. 1 and 2. Percentage cumulative frequency of vaccinated sheep accepting no more than the specified number of: total lesions (necrotic and viable) (Fig. 1) and viable cysts (Fig. 2) following a challenge infection with 2500 eggs of *E. granulosus*. Antigen: ——, activated embryos; – – –, viable eggs; ———, control. Species: ◇, *E. granulosus*; ○, *Taenia hydatigena*; △, *T. ovis*; □, *T. pisiformis*.

TABLE 6

THE PERCENTAGE EFFICIENCY OF HOMOLOGOUS AND HETEROLOGOUS EGGS AND ACTIVATED EMBRYOS IN PROTECTING SHEEP AGAINST THE ESTABLISHMENT AND SUBSEQUENT SURVIVAL OF *Echinococcus granulosus*

Parasite	Antigen	Challenge infection with *E. granulosus*	
		Immunity at the intestinal level	Immunity at the site of election
E. granulosus	Activated embryos	91·2**	96·0**
	Viable eggs	91·9**	100·0**
T. hydatigena	Activated embryos	31·3	89·0**
	Viable eggs	0·0	6·9
T. ovis	Activated embryos	38·4	97·4**
	Viable eggs	19·8	0·0
T. pisiformis	Activated embryos	0·0	19·3
	Viable eggs	0·0	0·0

** Significant at 1 per cent level.

The percentage immunity in each phase is calculated from the following:

Immunity at the intestinal level is $\left(1-\frac{N_t+V_t}{N_c+V_c}\right)\times 100$,

Immunity at the site of election is $\left(\frac{\frac{N_t}{N_t+V_t}-\frac{N_c}{N_c+V_c}}{1-\frac{N_c}{N_c+V_c}}\right)\times 100$,

where N_t = the number of necrotic lesions per animal within each test group; N_c = the number of necrotic lesions per animal within each control group; V_t = the number of viable cysts per animal within each test group; V_c = the number of viable cysts per animal within each control group.

A comparison of the percentage cumulative frequencies in Fig. 2 shows that for *E. granulosus*, both the activated embryo and eggs are slightly superior to the activated embryos of *T. ovis* and *T. hydatigena* in protecting the host against the long-term survival of hydatid cysts. The eggs of *T. hydatigena* and *T. ovis* form similar lines with the eggs and activated embryos of *T. pisiformis* and the controls and, therefore, these antigens give no obvious protection against the long-term survival of hydatid cysts at the site of election.

Table 6 shows the percentage protective efficiency of the various procedures used, together with their significance at the 1 per cent level. The activated embryos and eggs of *E. granulosus* induce a strong resistance to the establishment of the challenge infection of *E. granulosus*. These antigen complexes as well as those of the activated embryos of *T. hydatigena* and *T. ovis* also induce a strong resistance significant at the 1 per cent level against the survival of hydatid cysts at the sites of election.

COMPARATIVE VALUE OF THE AMOUNT OF ANTIGEN INJECTED IN PROTECTING SHEEP AGAINST *E. granulosus*

Table 7 shows the variations in the number of hydatid cysts established and surviving from the challenge infiltration compared with the number of eggs or activated embryos of each species injected as a vaccine. No apparent differences in average counts of total lesions from the challenge infection of *E. granulosus* were found between the different amounts of antigen given to the animals in any of the sub-groups in this trial.

TABLE 7

VARIATION IN THE NUMBER OF *Echinococcus granulosus* CYSTS ESTABLISHED BY CHALLENGE AND SURVIVING FOR 30 MONTHS IN SHEEP VACCINATED WITH HOMOLOGOUS AND HETEROLOGOUS HEXACANTH EMBRYOS

Species and antigen type		No. of viable and dead hydatid cysts in sheep immunized with: 1000	1000	2000	2000	5000	5000 eggs or embryos	20,000	20,000	50,000	50,000
E. granulosus											
Activated	a	4	2	1	Died	2	1	4	18	0	22
embryos	b	0	1	0		0	0	0	0	0	0
Viable eggs	a	6	3	15	Died	4	5	9	0	3	Died
	b	0	0	0	Died	0	0	0	0	0	Died
T. hydatigena											
Activated	a	91	24	165	4	20	2	59	Died	1	Died
embryos	b	0	0	0	0	8	0	7		2	
Viable eggs	a	36	34	19	Died	7	54	50	2	199	Died
	b	10	35	109		11	30	0	48	0	
T. ovis											
Activated	a	50	12	21	20	62	Died	12	177	26	0
embryos	b	0	1	0	3	0		0	0	0	0
Viable eggs	a	Died	Died	34	Died	0	37	13	3	4	63
	b			5		71	23	14	67	17	40
T. pisiformis											
Activated	a	80	22	4	67	20	70	16	1	159	63
embryos	b	20	47	56	12	0	7	96	0	0	6
Viable eggs	a	3	55	28	191	0	Died	1	Died	49	17
	b	17	17	68	0	1		99		39	19

a, No. of retarded and necrotic lesions; b, No. of viable cysts.

DISCUSSION

The results demonstrate that both the activated embryos and eggs of *E. granulosus* induce an equally strong immune response to the establishment and to the long-term survival of hydatid cysts in sheep. In one animal, one acephalocyst survived, but the volume of cyst fluid which accumulated within thirty months was less than 2 ml. This suggests that the immune response stimulated by the single injection of the homologous embryos exerts an effect throughout the cyst growth phase.

A previous cross-protection study in sheep in which *T. hydatigena* was used as the test challenge organism demonstrated that the activated embryo but not the egg of *T. ovis* induces protection against *T. hydatigena* (Gemmell, 1964). The results from the present study show that the activated embryos, but not the egg of these two sheep metacestodes also induce protection against *E. granulosus*.

A further cross-protection study (Gemmell, 1965a) showed that the eggs or activated embryos of *T. hydatigena* and *T. ovis* failed to induce any useful protection to a challenge infection of *T. pisiformis* in rabbits, and conversely, the eggs or embryos of *T. pisiformis* failed to protect sheep against these two sheep metacestodes. In the present study, the eggs or the embryos of *T. pisiformis* also gave no protection to *E. granulosus*.

Therefore, these studies indicate that there are at least two functional antigens. One complex is species specific and is contained in the viable egg of the homologous species. This complex induces resistance to the invading organism, possibly at the intestinal level. The other complex, responsible for cross-protection, is present in the activated embryo of some species of different genera parasitizing the same host. This complex exerts its effect mainly against the growing larval cyst at the site of election.

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