PARTIAL IMMUNOLOGICAL PARALYSIS TO *TRICHOMONAS FOETUS* ANTIGEN IN CALVES

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(With 4 Figures in the Text)

Trichomonas foetus is a flagellate parasite of the genital tract of cattle. While studying the reactions of very young calves to intramuscular injections of crude, freeze-dried, whole bodies of *T. foetus*, we observed no measurable response to injections given during the first 3 weeks of life. When very large amounts of antigen were given during this unresponsive period, the capacity of the animal to respond to the same antigen at a later age, when it would normally produce antibody, was seriously impaired.

The present account gives the later history of the four animals described in the earlier paper (Kerr & Robertson, 1954) and the details of a fifth treated in much the same way.

Our material and methods were those previously described (Kerr & Robertson, 1954), except that the agglutinating potency of the sera is expressed in two ways: the end-tube of +agglutination; and the intensity of agglutination which is expressed by the index, which is the sum of the plus signs assigned to each tube in the agglutination series starting as a routine at 1/6 and continuing in a two-fold dilution series.

Thus in the following series the titre is 1/96 and the index is 11:

1/6	1/12	1/24	1/48	1/96	1/192
+++(+)	++(+)	++	+(+)	+	(+)

Titres are recorded as the reciprocal of the dilution.

The normal agglutinin, when fully developed in animals of 8 months or more, has a titre of 96 and an index of 11–12. Agglutinins induced in normal animals by injection of antigen reach a titre of 768–3072 with a total index of 27–35.

'Normal agglutinins' (n.a.) are those found in all normal sera of cattle, horses, sheep, goats, rabbits and man for *T. foetus* (Kerr & Robertson, 1954).

'Induced antibody' is the agglutinin produced by the injection of *T. foetus* antigen. 'Immune paralysis' or partial paralysis indicates an impairment of the normal responsiveness to antigen analogous to that described by Felton (1949).

RESULTS

Four calves, H 8, H 9, P 8*c* and P 10*c*, were described in the earlier paper. They had received relatively large doses of antigen before the 21st day of life and produced no antibody as a result. The fifth calf, H 14, received more antigen, 4 g. between the

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3rd and 46th day, 2 g. between the 87th and 108th day, and after a pause of 83 days when it was 6 months old, 2 g. After none of these injections did it produce agglutinins. All five animals responded feebly when older to the standard injection of 2 g. in four doses. The response appeared to be due to induced antibody because the titres subsided again unlike the n.a. which remains steady. Thus H 8 and H 9 failed to respond at 6 months, but when they were $12\frac{1}{2}$ and $8\frac{1}{2}$ months old respectively, responded slightly but definitely, the index rising from between 11 and 12 to $17\frac{1}{2}$. After a rest of a further $11\frac{1}{2}$ months, they still reacted to challenge by this slight increase in titre.

P 8*c* and P 10*c* were similarly impaired, but P 10*c* reacted positively much earlier when 74 days old, though at this stage the evidence of impairment is not clear cut, because a normal animal of that age may also respond feebly. Tested when about 6 and 18 months old both animals behaved like H 8 and H 9 at $12\frac{1}{2}$ and $8\frac{1}{2}$ months with an impaired response.

H 14 tested when 12 and 20 months old reacted similarly on both occasions. The impairment was rather less in this animal than in the other four, the titre being 288 and the index 19–20.

The impaired reaction must be viewed in relation to the behaviour of normal animals. Fig. 1 shows the response of three animals given their first course of antigen at 3, 5 and 20 months. The first responds slightly but the second and third reach the full titres expected in adult cattle.

Fig. 2 shows two examples of animals having had antigen in early life, though not during the first 3 weeks of life, and which were not impaired; and Fig. 3 shows the reaction of three of the impaired animals. H 8 and P 10*c* responded feebly to the antigen and H 14, although 6 months old, did not produce a measurable amount of induced agglutinin. In Fig. 4, H 7, the normal control, shows the type of increase in the titre expected after a pause of $8\frac{1}{2}$ months, during which the agglutinins have dropped to very nearly the figure of the n.a., P 10*c* and H 14, two impaired animals, produce a low response to the antigen in spite of the long rest of $10\frac{3}{4}$ and $6\frac{1}{2}$ months respectively.

DISCUSSION

Hanan & Oyama (1954) observed that rabbits receiving injections of bovine serum in early life produced no antibody and failed to do so when given antigen at a later date. These authors contended that the formation of antibody to an unrelated antigen had also been influenced. Dixon & Maurer (1955) note that large doses of heterologous plasma protein injected into rabbits from birth onwards induced an unresponsiveness that lasted 10–11 months when the experiments were discontinued; the unresponsiveness was specific.

Cinader & Dubert (1955) induced unresponsiveness in rabbits to human albumen by injecting it into newborn rabbits. The behaviour of our animals differs in some respects from these examples. The calves were purposely given long periods of rest, and whereas H 14 was still unresponsive at 6 months, like all the rest, it finally responded to the antigen. The animals' capacity to produce antibody was definitely

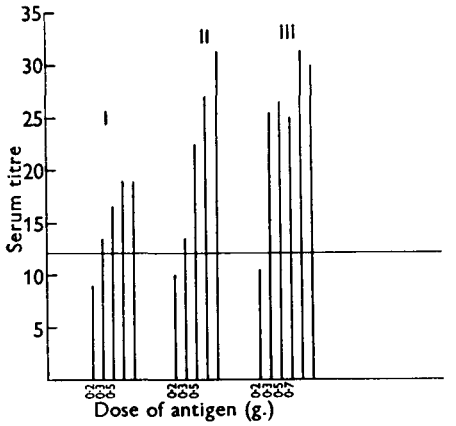

Fig. 1

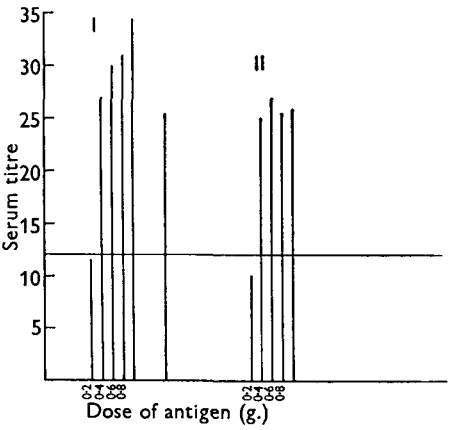

Fig. 2

Fig. 1. Primary responses to antigen at different ages in normal animals: I, H 7, 3 months; II, K 7*c*, 5½ months; III, K 9, 20 months. The ordinates represent the titres of the sera in terms of the index. The doses of antigen were given 7 days apart and the serum was taken for the tests immediately before the injection of the antigen. Where in these figures the lines indicating the titre are farther apart it signifies that the times of taking samples were separated by multiples of 7 days. The horizontal line across the figures represents the average index of the normal agglutinin.

Fig. 2. Responses to antigen in animals having had antigen in early life but not impaired. I, H 7, 0·5 g. at 96th to 287th day; reinjected at 15½ months; II, K 10*c*, 0·9 g. at 29th to 72nd day; reinjected at 17½ months.

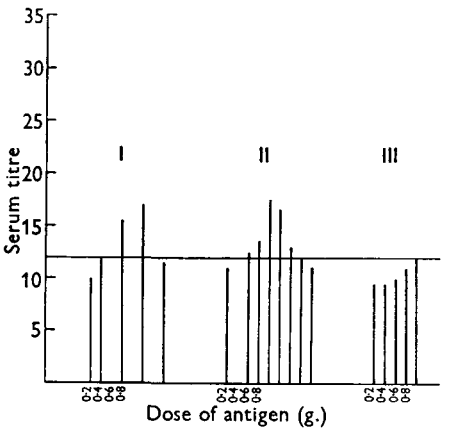

Fig. 3

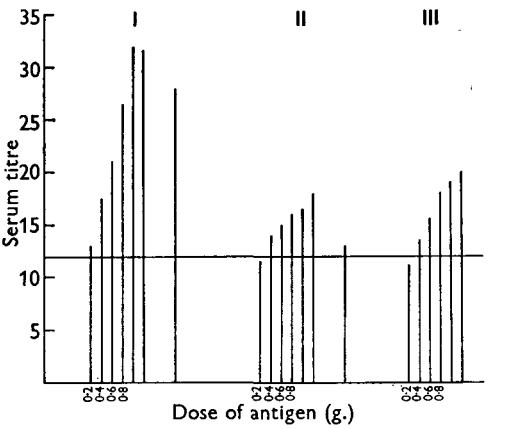

Fig. 4

Fig. 3. Impaired response to antigen in animals treated with large amounts of antigen in early life. I, H 8, 3 g. at 8th to 79th day; 0·9 g. at 193rd day to 242nd day; reinjected at 12½ months; II, P 10*c*, 2 g. at 7th to 23rd day; 1·5 g. at 74th to 94th day; reinjected at 6 months. III, H 14, 4 g. at 3rd to 52nd day; 2 g. at 87th to 108th day; reinjected at 6 months.

Fig. 4. Response to antigen of normal and impaired animals reinjected after a period of rest. I, H 7, normal animal, 3·5 g. at 96th to 287th day; 2 g. at 15½ months; reinjected at 26 months; II, P 10*c*, impaired animal, 2 g. at 7th to 23rd day; 2 g. at 74th to 94th day; 2 g. at 6 months; reinjected at 17 months; III, H 14, impaired animal, 4 g. at 3rd to 52nd day; 2 g. at 87th to 108th day; 2 g. at 6 months; reinjected at 20 months.

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impaired, but it was not completely abolished. As we stated in the previous paper, the serological test system we have to use is not a good one for detecting small amounts of induced antigen, as it may be obscured by the normal agglutinin. Our failure to produce complete paralysis may have been due to minor antigens present in our crude freeze-dried *T. foetus* antigen. The large doses given in very early life would paralyse the response to the major antigen, but might leave responses to the minor antigens relatively unimpaired.

The investigators we have cited do not seem to have observed the partial breakdown of the paralysis we have met, though an animal, 695E in the series of Cinader & Dubert, would seem to be an example.

The work of Billingham, Brent & Medawar (1953, 1955) with skin grafts has much in common with all these examples of inhibition of immunological response. Moreover, the ultimate breakdown of the inhibition and the rejection of the grafts in many of their animals suggests a further resemblance with the partial inhibition in the calves, but the analogy of the immunological unresponsiveness and the tolerance of the grafts produced by the injection of live tissue into embryos is not complete.

The correspondence between the two sets of results is not clear because the living cells might be, to some extent, incorporated as part of the permanent tissue of the embryo receiving the injection.

SUMMARY

The intramuscular injection of large amounts, 2–3 g., of *Trichomonas foetus* crude antigen into five young calves during the first 3 weeks of life produced no antibody.

When the animals were tested with the standard challenge at intervals of several months they responded feebly, showing a definitely impaired capacity to produce antibody, when compared with the response of normal animals.

The ages of the animals still showing this partial paralysis ranged from 1 year and 5 months to 2 years and 2 months.

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