Zeitschrift: Acta Tropica
Herausgeber: Schweizerisches Tropeninstitut (Basel)
Band: 38 (1981)
Heft: 1

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DOI: https://doi.org/10.5169/seals-312801

Acta Tropica *38*, 15–28 (1981)

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The dynamics of the cellular reactions elicited in the skin of goats by *Glossina morsitans morsitans* infected with *Trypanosoma (Nannomonas) congolense* or *T. (Duttonella) vivax*

D. L. Emery, S. K. Moloo

Summary

Local skin reactions were elicited in goats by tsetse infected with either *T. (N.) congolense* or *T. (D.) vivax*. For the former trypanosomes, the skin reaction was detected initially 7 days after challenge and was maximal 3 days later. Histologically, the cellular response involved an initial influx of polymorphonuclear leucocytes (PMN) which was followed by a substantial infiltration of lymphocytes and macrophages. Large numbers of plasma cells remained in the skin reaction during its decline. Moderate numbers of parasites were observed in lesion at the height of the reaction.

T. (D.) vivax provoked a small nodular skin reaction which became apparent 7 days after challenge. The cellular response, which peaked on day 9, contained large numbers of lymphocytes and macrophages and only a small contribution from PMN. Only small numbers of trypanosomes were observed in the chancre. The skin reaction elicited in goats by *T. (N.) congolense*, *T. (D.) vivax* or *T. (T.) brucei* were mutually distinct in their morphological appearance and size at the peak of the response, and in the interval required after challenge to attain maximum dimensions.

Key words: Trypanosoma (Nannomonas) congolense; T. (Duttonella) vivax; Glossina morsitans morsitans, goats; skin reaction.

Introduction

A local skin reaction, termined the "chancre", has been described in several domestic animals and man as the initial response of the susceptible difinitive

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host to infection with African trypanosomes by the tsetse fly. The trypanosomal species which have been reported as eliciting a chancre include *T. (T.) rhodesiense* (Fairbairn and Godfrey, 1957), *T. (N.) congolense* (Roberts et al., 1969) and *T. (T.) brucei* (Willett and Gordon, 1957; Emery and Moloo, 1980).

The chancre appears to restrict initially the systemic migration of the trypanosomes in that parasites can be demonstrated in the skin at the site of challenge prior to their detection in the bloodstream (Willett and Gordon, 1957; Luckins and Gray, 1978; Emery and Moloo, 1980). This localization of the parasite is probably advantageous to the host for the priming of its immune systems, and to the trypanosome for the generation of variable antigenic types (VATs). A detailed histological analysis of the chancre was considered necessary as part of a study to assess the role of the tissue response in the pathogenesis of African trypanosomiasis. Previously, Emery and Moloo (1980) investigated the cellular changes in the chancre elicited by *T. (T.) brucei.* This paper describes a comparative study of the sequential histological changes in the skin of goats challenged by *Glossina* infected with *T. (N.) congolense* or *T. (D.) vivax.*

Materials and methods

1. Animals and infection

Goats: Fourteen male East African goats (Masai × Galla cross-breds) aged 12 months and weighing 20–25 kg were housed in insect-proof isolation units and were allowed free access to hay and water.

Trypanosomes: T. (N.) congolense, ILRAD stabilate 285 was used to infect tsetse in the present experiment. This stabilate was derived from ILRAD stabilate 13-E8 (Emery et al., in press) by a single cyclical transmission through A/J mice, and has been used to elicit local skin reactions in cattle following challenge with infected tsetse (Akol, unpublished).

The stock of *T. (D.) vivax* (ILRAD 417) used was a derivative of Zaria Y486 (Leeflang et al., 1976). After several passages in mice and two cows, Zaria Y486 was cyclically passaged between goats via infected *G. m. morsitans* and cryopreserved as stabilate ILRAD V17. The stock ILRAD 417 is a derivative of ILRAD V17.

Infection of tsetse

Fifteen NMRI mice were each injected intraperitoneally (i.p.) with *T. (N.) congolense* (ILRAD 285). Teneral *G. m. morsitans* (352 ♂♂) from R6 ILRAD colony (Moloo, 1979) were fed on these mice when they showed a parasitaemia of 10^6 per ml which was on day 12–13 after inoculation. The tsetse were maintained on rabbits screened daily as negative for trypanosomes. After 23 days, tsetse were allowed to probe singly on warm slides at 37° C to identify those with mature infection for subsequent challenge.

Sixty *G. m. morsitans* (10-day old males) were fed on a goat which had been injected i.m. with *T. vivax* ILRAD 417 when the parasitaemia reached 10^5 per ml on day 8. Experience with this *T. (D.) vivax* has shown that tsetse with metatrypanosomes in their hypopharynx do not readily extrude these parasites with saliva by the warm-slide probe technique. Hence, on day 21 after the infected food intake, the tsetse were grouped into batches each comprising 10 tsetse. These batches of tsetse were fed individually on 6 different goats and then dissected. Twenty-nine of the 60 tsetse were found to be infected, an infection rate of 48.3%.

Experimental design

a) *T. (N.) congolense:* Six goats were each challenged with 4 infected tsetse, 2 on each clipped flank, and the 'bites' were marked. The challenge elicited 23 chancres.

b) *T. (D.) vivax:* Following the successful induction of 3 local skin reactions in a goat by 3 tsetse infected with a derivative of *T. (D.) vivax* ILRAD V17, 6 goats were each challenged with 10 tsetse infected with ILRAD 417 as described above. The position of each 'bite' was numbered and marked to correlate with the respective tsetse used. Twenty-six reactions resulted from the bites of 29 infected tsetse and no macroscopic lesions appeared from the bites of tsetse which were recorded as uninfected after subsequent dissection. The number of reactions which appeared on the goats was 3, 4, 4, 4, 5 and 6. On 2 of the goats, all of the chancres were located only on one flank.

2. Sampling techniques

Daily measurements of skin thickness, the size of regional lymph nodes, parasitaemia and the sequential sampling of skin biopsies from the chancre were conducted as described previously (Emery and Moloo, 1980). A skin biopsy was taken from each of 2 goats on days 0, 4, 7, 8, 9, 10, 11, 13, 14, 15 and 22 for infection with *T. (N.) congolense* and days 0, 4, 8, 9, 10, 13 and 22 for infection with *T. (D.) vivax.*

3. Quantitative histology

Skin biopsies were placed in Bouin's fixative and were processed by conventional methods. The blocks were placed in Celloidin (in methyl benzoate) before embedding in paraffin wax. Sections 3–5 μm thick were cut from the paraffin-embedded tissue and were stained with either Giemsa or Mayer's haemotoxylin and eosin. Total cellularity of tissue sections and quantitative cellular histology were determined from 4 sections of each biopsy as described previously (Emery and Moloo, 1980). The number of different cell types were expressed per mm^2, and the number of trypanosomes were scored as follows: + = 5–50 trypanosomes per mm^2; + + = 50–250 trypanosomes per mm^2; + + + = 250–500 trypanosomes per mm^2; + + + + = greater than 500 trypanosomes per mm^2.

Results

Clinical course of the chancre

1. *T. (N.) congolense:* The local skin reaction which developed from the bite of tsetse infected with *T. (N.) congolense* was first detected as a palpable discrete nodule 6–7 days after challenge (Fig. 1). The reaction progressively attained, by day 10, the appearance of a more diffuse raised plaque with substantial subcutaneous oedema, heat and pain. The appearance and development of the chancre was accompanied by a pronounced enlargement of the regional lymph node. After day 10, the reaction subsided rapidly and 5 days later the skin thickness had returned close to the dimensions of normal skin which was maintained until death of the hosts 25–40 days after challenge. The skin thickness increased from 4.0 mm to reach 8.7 mm at the peak of the response on day 10 (Fig. 1). During the same period the cellular content of the skin involved in the local swelling had increased 10–15 times greater than that of normal skin. The appearance of the chancre preceded by 3–4 days, the initial detection of *T. (N.)*

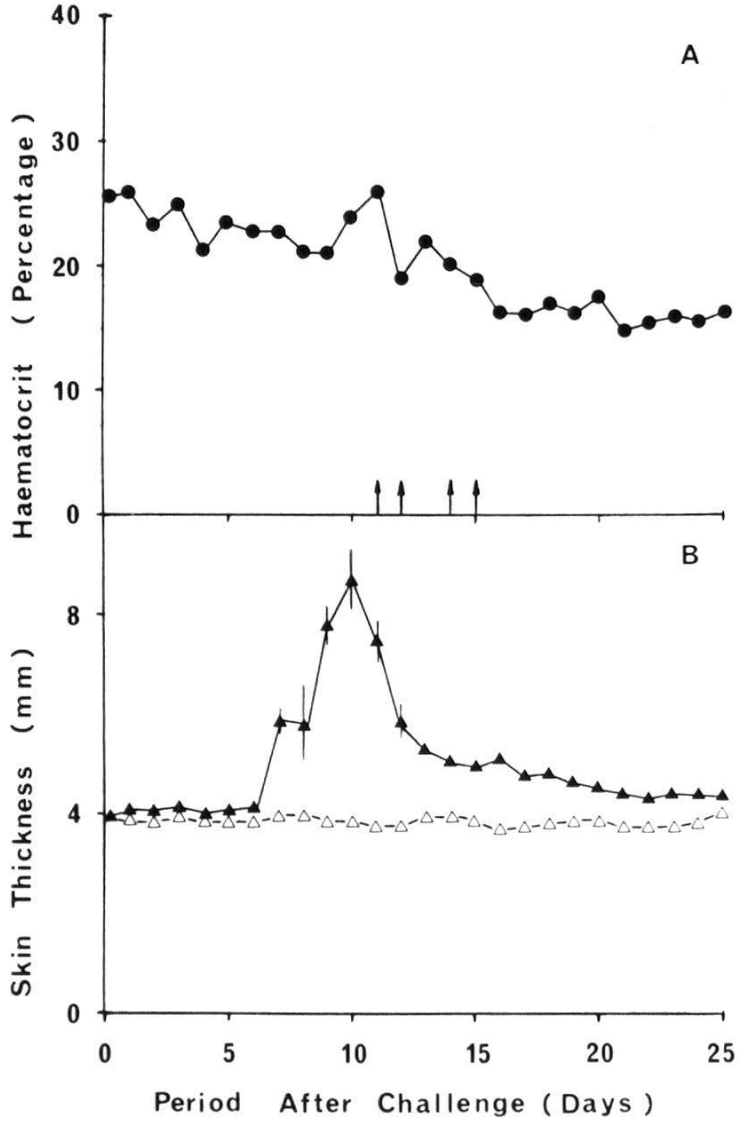

Fig. 1. Changes in haematocrit (A) and skin thickness (B) of 6 goats following challenge with tsetse infected with *T. (N.) congolense*. Parasitaemia was detected initially (↑) in goats on days 11 (2), 12 (2), 14 (1) and 15 (1). The goats died on days 26, 28, 31, 35, 38 and 40. ● = changes in haematocrit; △ = bites of uninfected tsetse; ▲ = bites of infected tsetse (± SD).

congolense in peripheral blood (greater than $6–8 \times 10^3$ per ml) 9–11 days after challenge (Fig. 1). The haematocrit declined steadily from an initial average of $26 \pm 2.4\%$ (± S.D.) to less than 16% in moribund goats.

2. *T. (D.) vivax:* In comparison with the chancres elicited by *T. (N.) congolense* and *T. (T.) brucei* (Emery and Moloo, 1980) those elicited by *T. (D.) vivax* were the least spectacular (Fig. 2). Skin thickness increased from 6 days after challenge to peak 3 days later at an average thickness of 6.0 mm which represented 50% increase above normal. The reaction declined slowly over the ensuing 6 days and the skin had resumed normal dimensions when the hosts died between 16 and 25 days after challenge. Throughout its development and decline, the local skin reaction presented as a raised, discrete nodular swelling, with minimal subcutaneous oedema, but moderate heat and pain. The appear-

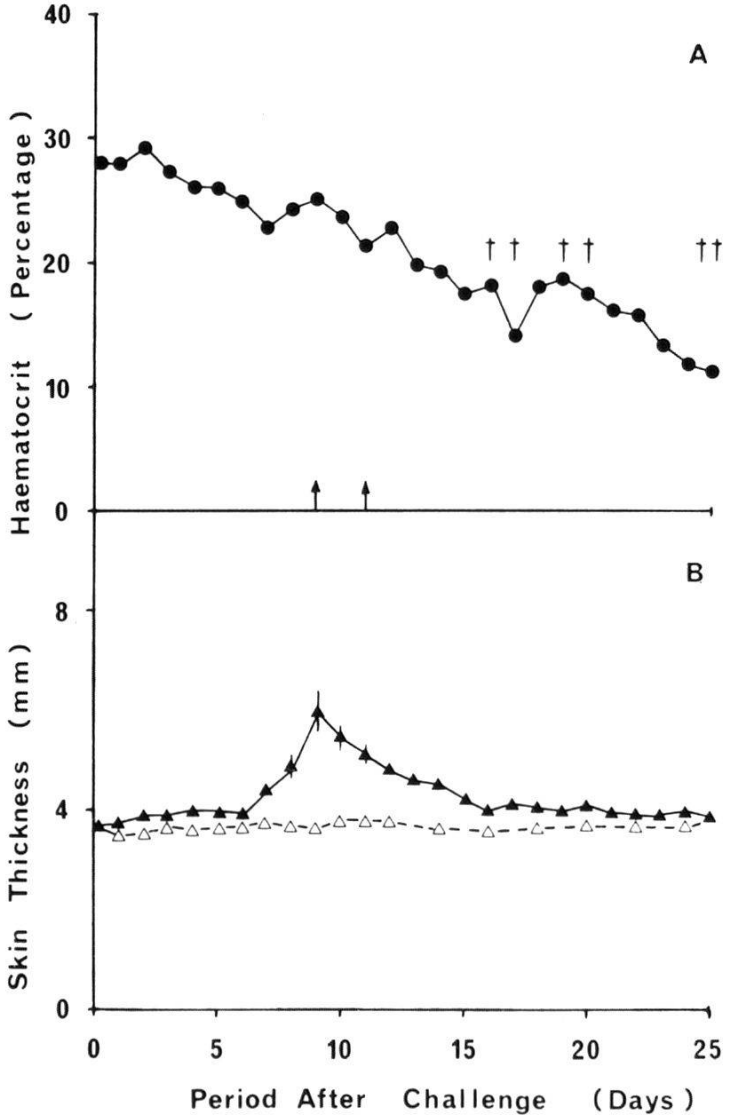

Fig. 2. Changes in haematocrit (A) and skin thickness (B) of 6 goats following challenge with tsetse infected with *T. (D.) vivax*. Parasitaemia was detected initially (↑) in goats on days 9 (1) and 11 (5). ● = changes in haematocrit; △ = bites of uninfected flies; ▲ = bites of infected flies (±SD); † = death of host.

ance of the chancre preceded by only 12–24 h, the first demonstration of trypanosomes in the bloodstream (Fig. 2). From an initial level of 30 ± 1.8%, the hematocrit decreased progressively throughout the infection to less than 20% in moribund goats.

Chancres initiated by both *T. (D.) vivax* and *T. (N.) congolense* induced marked enlargement of the regional lymph nodes (prefemoral nodes). At necropsy on moribund animals, the regional lymph nodes of 2 goats infected with *T. (N.) congolense* weighed 10.1 ± 2.6 g (±S.D.) in comparison with the weight of 4.5 ± 1.8 g for the prefemoral LN from 6 normal goats. The corresponding weights from the 2 goats whose chancres from *T. (D.) vivax* appeared only on 1 flank were 10.3 ± 2.6 g for the regional LN and 5.8 ± 1.6 g for the contralateral LN.

1. Detection of trypanosomes in tissue sections. T. (N.) congolense were detected histologically in chancres from 7 days after the feeding of infected tsetse (Table 1). Moderate numbers of parasites (150–250 per mm^2) were observed between collagen fibres and throughout the inflammatory oedema until the 15th day after challenge. Trypanosomes were more numerous in the deeper structures of the dermis during the early development of the chancres, but appeared later to be distributed more evenly throughout the tissue reaction.

Only small numbers of parasites were found in the respective chancres elicited by *T. (D.) vivax* (Table 2). Trypanosomes were occasionally found (approximately 5–10 per mm^2) between 6 and 15 days after challenge only in the deeper dermal tissue between collagen fibres and within the tissue oedema. Parasites were scarce in skin biopsies sampled after day 15. However, large numbers of trypanosomes (200–300 per mm^2) were observed between collagen fibres in the superficial dermis in sections obtained from both the sites of challenge and elsewhere on day 13 (Fig. 7) and when the goats were moribund (around day 22). Both these periods corresponded respectively to the first and second peaks of parasitaemia in the hosts, and it was considered that trypanosomes from the bloodstream were responsible for the increase in skin reactions. Goats succomb to infection with this stock of *T. (D.) vivax* at the first or second peak of parasitaemia.

2. Quantitative cellular changes in the skin. a) *T. (N.) congolense:* During the first 7 days after inoculation of the metatrypanosomes of *T. (N.) congolense*, relatively minor changes in the proportions and absolute numbers of cells were observed in skin sections sampled from the site of challenge (Table 1). Thereafter a marked inflammatory response, characterized by the infiltration of polymorphonuclear leucocytes (PMN), lymphocytes and macrophages contributed to the development of the chancre. The initial increases in skin thickness which occurred at days 8 and 9 were accompanied histologically by a massive extravasation of PMN (500–550 per mm^2) into the dermal connective tissue; an incursion more pronounced in the deeper areas of the dermis. The cellular response occurred concurrently with substantial oedema and vascular congestion in the surrounding tissues resulting in disruption of the structural morphology of collagen bundles (Fig. 3). Afferent lymphatic vessels appeared distended with amorphous proteinaceous material in which an occasional trypanosome was detected. At the peak of the tissue reaction on day 9–10, numerous degenerating PMN were observed in the deeper dermis and large numbers of mononuclear leucocytes accumulated in the perivascular areas (Fig. 4). The extravasation was accompanied by the emigration of macrophages (up to 900 per mm^2) from dermal vessels. Within 24 hours, lymphocytes and macrophages were detected in increased numbers throughout the dermal tissue involved in the inflammatory reaction. PMN maintained their presence at approximately 50–150 per mm^2

Table 1. Cellular changes in the skin reaction elicited by *Trypanosoma congolense*

Location and cell type	Period after challenge (days)								
	0	4	7	8	9	10	13	15	22
Trypanosomes	−	−	+	+	++	++	++	+	−
Dermal:									
Cells per field	480	763	1070	3530	3419	3100	2644	1697	1427
PMN	2.5 (0.5)	4 (0.5)	50 (4.5)	549 (15)	496 (14)	578 (18)	178 (6.5)	44 (2.5)	14 (1)
Lymphocytes	129 (26)	142 (18)	283 (25.5)	1276 (32)	1276 (36)	1108 (34.5)	1042 (38)	493 (28)	355 (24)
Plasma cells	174 (35)	111 (14)	155 (14)	293 (8)	284 (8)	193 (6)	233 (8.5)	176 (10)	310 (21)
Macrophages	25 (5)	40 (5)	50 (5)	183 (5)	284 (8)	305 (9.5)	384 (14)	167 (9.5)	89 (6)
Fibroblasts	132 (27)	443 (56)	299 (27)	439 (12)	425 (12)	353 (11)	425 (15.5)	484 (27.5)	384 (26)
Others	85 (17)	134 (7)	266 (24)	1024 (28)	780 (22)	674 (21)	480 (17.5)	396 (22.5)	325 (22)
Perivascular:									
Cells per field	590	1193	1919	4736	5474	5362	4883	5806	4772
PMN	6 (1)	6 (0.5)	129 (6.5)	393 (8)	369 (6.5)	668 (12)	126 (2.5)	60 (1)	49 (1)
Lymphocytes	244 (40)	445 (36)	666 (33.5)	2356 (48)	3035 (53.5)	2585 (46.5)	2885 (57)	2497 (41.5)	1435 (29)
Plasma cells	196 (32)	260 (21)	269 (13.5)	196 (4)	114 (2)	250 (4.5)	177 (3.5)	842 (14)	1039 (21)
Macrophages	6 (1)	74 (6)	189 (9.5)	589 (12)	766 (13.5)	889 (16)	683 (13.5)	600 (10)	594 (12)
Fibroblasts	54 (9)	118 (9.5)	328 (16.5)	295 (6)	255 (4.5)	167 (3)	278 (5.5)	481 (8)	247 (5)
Others	102 (17)	340 (27.5)	408 (20.5)	1080 (22)	1135 (20)	1000 (18)	962 (18)	1534 (25.5)	1583 (32)

Numbers of each cell type are expressed per mm^2 from 4 sections of each of 2 goats. Percentages of each cell type are in parentheses. PMN = polymorphonuclear leucocytes.

Table 2. Cellular changes in the skin reaction produced by *Trypanosoma vivax*

Location and cell type	Period after challenge (days)							
	0	4	6	8	9	10	13	22
Trypanosomes	−	−	−	+	+	+	+++	++
Dermal:								
Cells per field	517	676	1156	1550	3456	2694	2595	2042
PMN	2.6 (0.5)	3.2 (0.5)	6 (0.5)	32 (2)	179 (5)	28 (1)	54 (2)	11 (0.5)
Lymphocytes	150 (28)	112 (16)	270 (22.5)	418 (26)	1110 (31)	796 (28.5)	686 (25.5)	423 (20)
Plasma cells	177 (33)	14 (2)	6 (0.5)	111 (7)	287 (8)	349 (12.5)	498 (18.5)	635 (30)
Macrophages	21 (4)	28 (4)	114 (9.5)	284 (19)	591 (16.5)	419 (15)	350 (13)	212 (10)
Fibroblasts	150 (28)	377 (54)	576 (48)	348 (22)	752 (21)	642 (23)	565 (21)	466 (22)
Others	73 (17)	168 (24)	228 (19)	395 (25)	663 (18.5)	558 (20)	538 (20)	381 (18)
Perivascular:								
Cells per field	517	934	2410	4674	4538	4145	3948	3050
PMN	11 (2)	5 (0.5)	25 (1)	24 (0.5)	94 (2)	65 (1.5)	20 (0.5)	16 (0.5)
Lymphocytes	220 (41)	296 (30.5)	950 (38)	2180 (45)	2282 (48.5)	1590 (37)	1387 (34)	664 (21)
Plasma cells	166 (31)	247 (25.5)	362 (14.5)	315 (6.5)	236 (5)	451 (10.5)	593 (14.5)	1107 (35)
Macrophages	11 (2)	58 (6)	175 (7)	945 (19.5)	917 (19.5)	664 (15)	553 (13.5)	348 (11)
Fibroblasts	54 (14)	287 (11.5)	339 (7)	282 (6)	403 (9.5)	389 (9.5)	285 (9)	285 (9)
Others	80 (14)	271 (28)	700 (28)	1066 (22)	800 (17)	1139 (25.5)	1166 (28.5)	759 (24)

Number of each cell type are expressed per mm^2 from 4 sections of each of 2 goats. Percentages of each cell type are in parentheses. PMN = polymorphonuclear leucocytes.

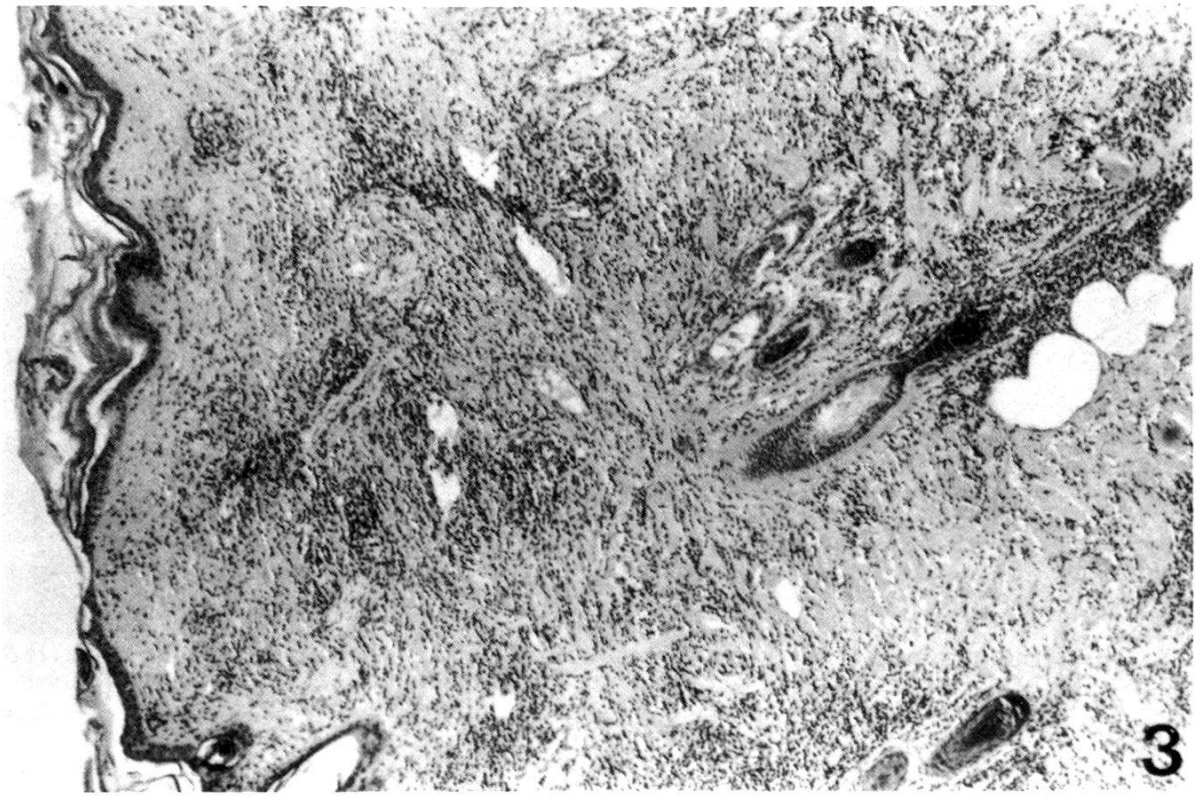

Fig. 3. Cellular infiltration into the skin reaction produced by *T. (N.) congolense* 14 days after challenge (H & E, $\times 50$).

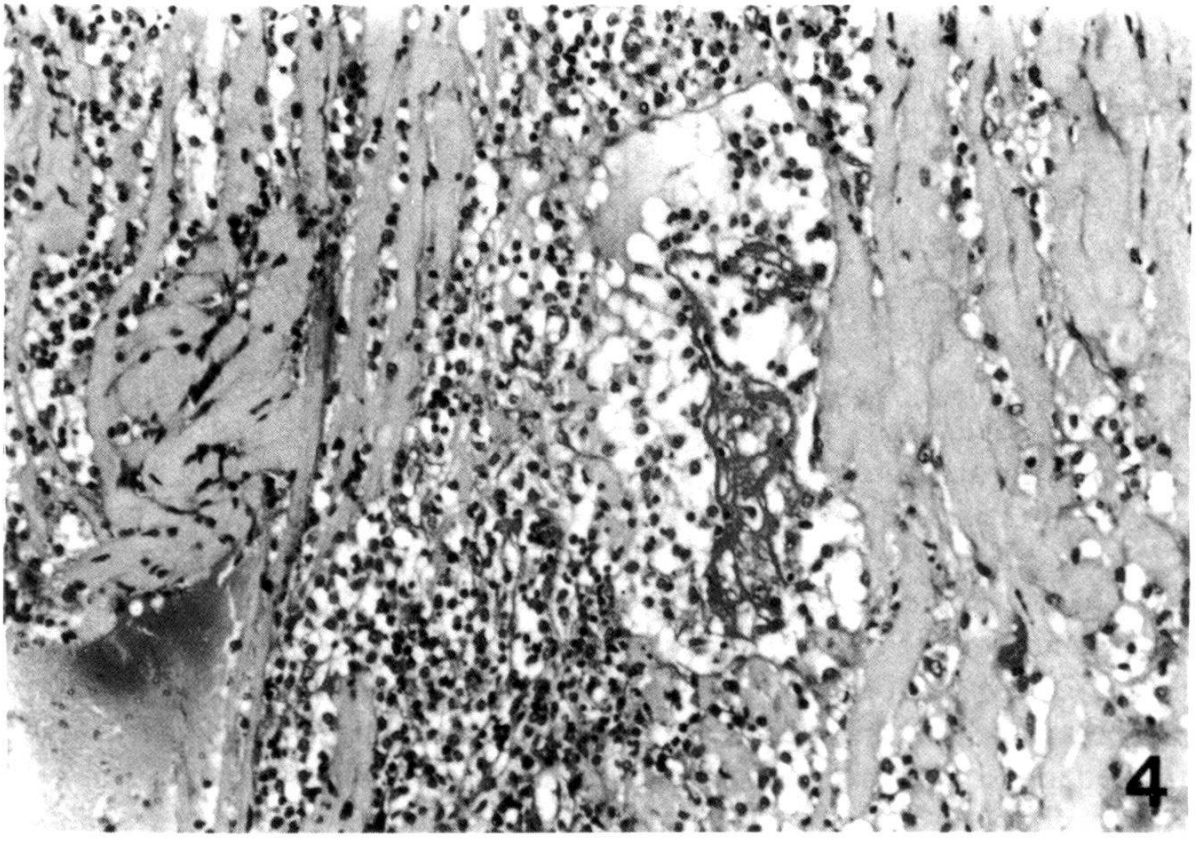

Fig. 4. Perivascular accumulations of lymphocytes, polymorphonuclear leucocytes and macrophages in the dermis 14 days after challenge with *T. (N.) congolense* (H & E, $\times 200$).

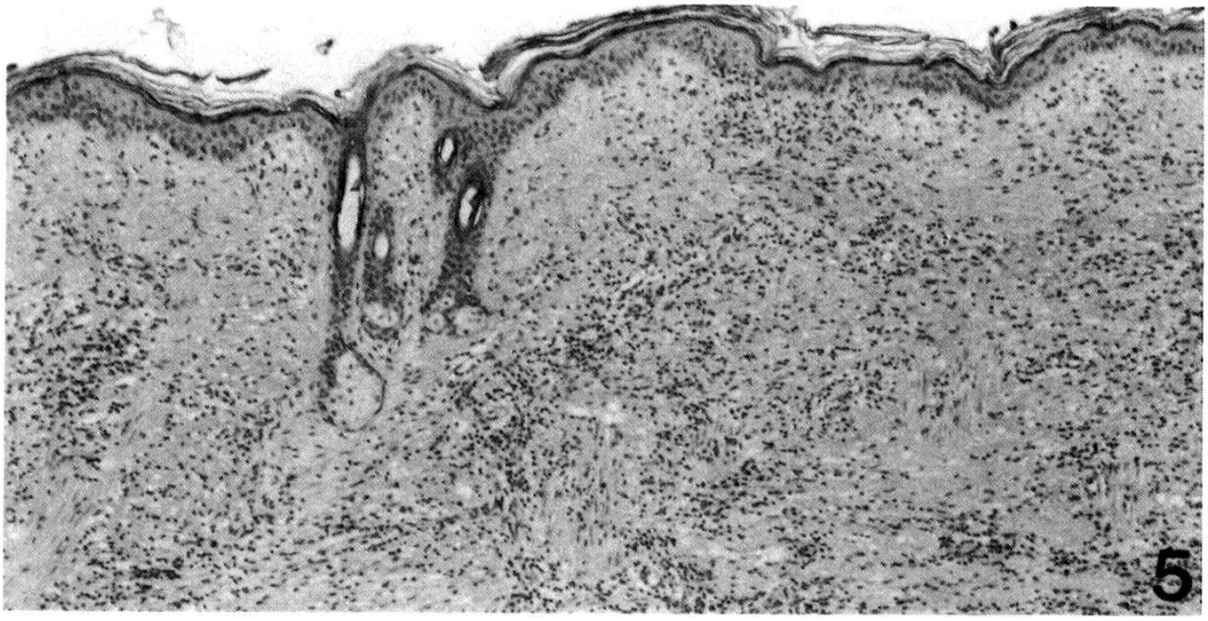

Fig. 5. Cellular infiltration into the skin reaction induced by *T. (D.) vivax* 8 days after challenge (H & E, ×50).

in the dermal connective tissue during the decline of the chancre, which was accompanied by decreases in the numbers of lymphocytes and macrophages, and progressive increases in the population of lymphoblasts and plasma cells. By days 14–15, higher numbers of eosinophils and mast cells (approximately 50–100 per mm^2 of both cell types) were observed perivascularly within the dermal stroma. In addition to these cell types, increased numbers of plasma cells, lymphoblasts and macrophages were still present in tissue sections sampled from goats in the terminal stages of the infection. During the decline of the tissue reaction, reparative influences characterised by the proliferation of tissue fibroblasts and vascular endothelial cells were evident in the deeper structures of the dermis.

b) *T. (D.) vivax:* The cellular populations in the skin at the site of infection with *T. (D.) vivax* remained relatively constant for the first 4 days after challenge except for a rapid decline in the numbers of plasma cells (Table 2). By day 6, perivascular accumulations of mononuclear leucocytes were evident in deeper areas of the dermis, whereas PMN were present in only small numbers in these locations (approximately 25 per mm^2). During the early stages of the cellular reaction, the response appeared to involve the deeper dermal connective tissue and to encroach progressively on the superficial layers of the dermis with the subsequent development of the chancre. The integrity of the dermal collagen was not substantially disrupted during the formation of the chancre, and the degree of vascular congestion and tissue oedema was reduced in comparison with that which accompanied infection with *T. (N.) congolense* (Fig. 5).

During the period which encompassed the height of the local lesion (from 6–10 days after challenge), the cellular reaction involved principally lympho-

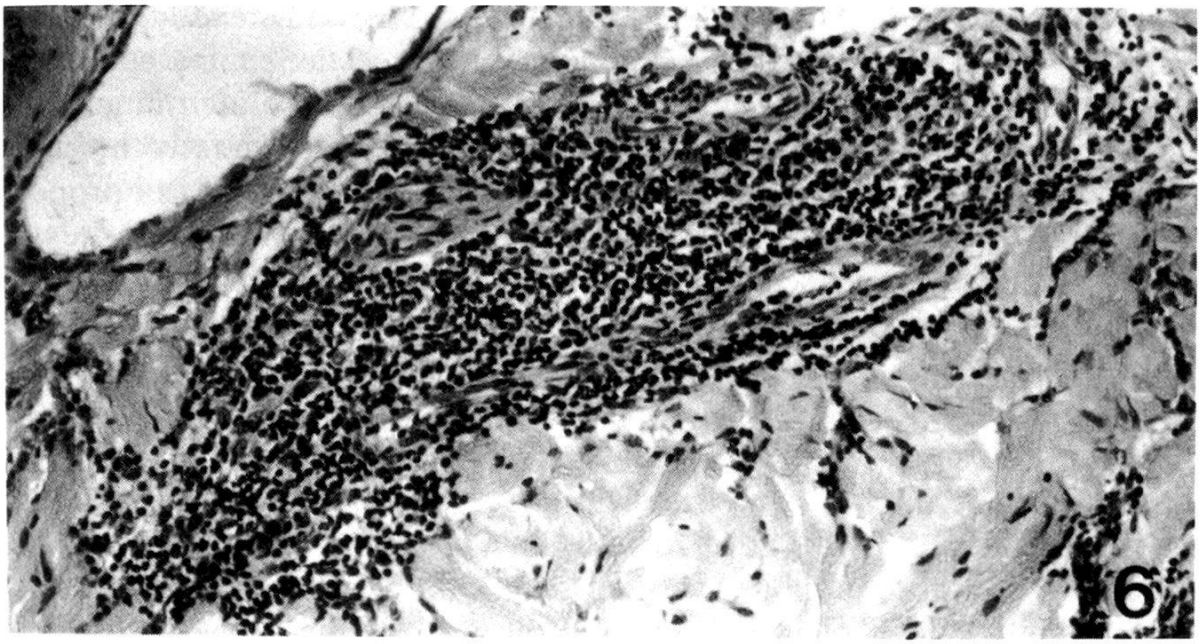

Fig. 6. Mononuclear cell infiltrate in the superficial dermis 8 days after challenge with *T. (D.) vivax* (H & E, ×180).

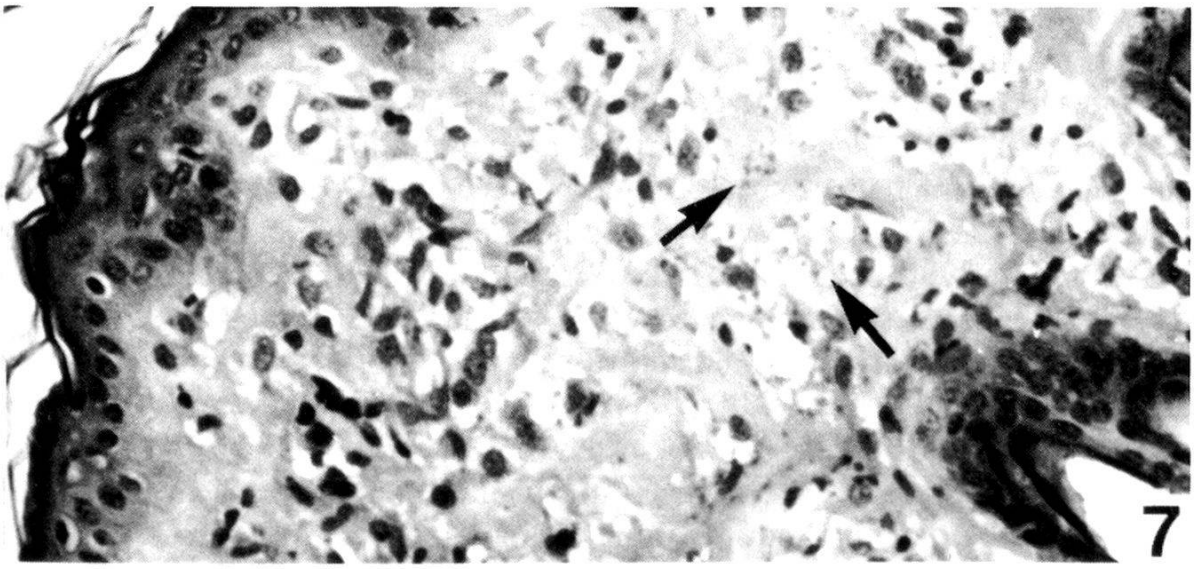

Fig. 7. Trypanosomes (arrow) in the superficial dermis of the skin reaction elicited by *T. (D.) vivax* 13 days after challenge (H & E, ×300).

cytes and macrophages. Both cell types appeared initially in perivascular infiltrates (Fig. 6), to be found later in increasing numbers in connective tissue throughout the dermis. Lymphocytes increased from 950 to 2300 per mm^2 in perivascular areas, and a similar proportional increase was observed in the dermal stroma. Macrophages were evident particularly in the immediate vicinity of dermal venules around day 9, but an increasing population in the connective tissue was also observed during this period. PMN did not contribute more than 5% of the total cellular content of the chancre at any stage of the response.

The proportions of lymphoblasts and plasma cells increased steadily after the peak of the tissue reaction and were prominent in skin sections sampled during the terminal stages of the infection (days 18 to 22). The absolute numbers of other cell types such as mast cells and eosinophils did not alter greatly throughout the duration of the skin reaction. In comparison, the numbers and proportions of cells observed in sections taken at similar intervals from the sites of challenge with uninfected tsetse approximated those observed in normal skin.

Discussion

Local skin reactions were elicited in goats following the inoculation of metatrypanosomes by tsetse infected with *T. (N.) congolense* or *T. (D.) vivax*. The lesions were more pronounced after infection with *T. (N.) congolense* although the interval between infection and the peak of the skin reaction was similar for both parasites (9–10 days).

As a sequel to the 'bites' of infected tsetse, *T. (N.) congolense* has been reported to elicit chancres in rabbits, sheep and cattle (Gray and Luckins, 1979; Murray et al., 1979), where the interval between infection and the height of the local skin reaction was similar to that observed in the present study. Given the similarities in the sequential development of the chancre associated with infection with *T. (N.) congolense* in several domestic animals, a similar pattern of cellular changes might be expected. The present investigation implicated the involvement of PMN, lymphocytes and macrophages whereas in cattle, Gray and Luckins (1979) described the local cellular responses as containing principally lymphocytes and macrophages. More recently, Akol (in preparation) observed from days 6–8 a substantial contribution of PMN to the chancre elicited by *T. (N.) congolense* in cattle.

The induction by *T. (D.) vivax* of local skin lesions in domestic livestock has not been reported previously, although in this laboratory Akol (unpublished) has observed the development of similar reactions in cattle infected with the same stabilate of *T. (D.) vivax*. In comparison with the reactions elicited in goats by *T. (N.) congolense* and *T. (T.) brucei* (Emery and Moloo, 1980), the lesion induced by *T. (D.) vivax* was the least dramatic, and involved the participation of lymphocytes and macrophages, with a minimal contribution of PMN. While histology is a relatively insensitive technique for the demonstration of parasites in tissue reactions, a comparison of the parasitic populations of each of the 3 trypanosomal species in the chancre revealed that the numbers declined respectively in the order *T. (T.) brucei, T. (N.) congolense* and *T. (D.) vivax*. A similar progression in the intensity and duration of the tissue reaction was also observed. Moreover, the features of the local skin reactions to each of *T. (T.) brucei, T. (N.) congolense* and *T. (D.) vivax* in goats are essentially similar, differences being apparent only in the relative contribution of PMN to each of the

chancres. The involvement of PMN appeared to parallel the development of a more florid inflammatory reaction and the appearance of substantial tissue oedema. This effect is probably related non-specifically and quantitatively to the numbers of respective trypanosome in the chancre.

However, the ultimate size of the chancre may also depend on the ability of the respective trypanosome to proliferate in an extra-vascular location, or to exit from the lesion into the systemic circulation. Following intradermal inoculation, bloodstream forms of *T. (T.) brucei* multiply locally and induce a skin reaction (Willett and Gordon, 1957), whereas a similar injection of up to 10^7 *T. (N.) congolense* elicit no response (Emery and Akol, unpublished). The smaller size of the chancre provoked by *T. (D.) vivax* and the smaller numbers of trypanosomes detected histologically within the lesion may reflect the initial numbers of metatrypanosomes inoculated by the tsetse. Based on daily examinations of saliva, Otieno and Darji (1979) suggested that tsetse extrude fewer *T. (D.) vivax* than *T. (N.) congolense. T. (D.) vivax* in the main attach on the inner wall of the hypopharynx (Moloo and Kutuza, 1977) while *T. (N.) congolense* are largely free at this site in the vector (Moloo, unpublished). Hence, the former are probably not easily dislodged during feeding. In comparison, tsetse infected with *T. (T.) brucei* extrude markedly greater numbers of metatrypanosomes than flies infected with *T. congolense* (Moloo, unpublished data) and the chancre appears 3–4 days earlier in goats infected with the former trypanosome (Emery and Moloo, 1980).

While the cellular components of the chancre throughout its development and decline in domestic livestock are relatively independent of host and trypanosome, the ultimate outcome of the infection is not. For example, the stabilates of *T. (N.) congolense* and *T. (D.) vivax* used in these experiments prove rapidly lethal for goats, whereas cattle either suffer a lengthy illness or abrogate the infection. It is therefore essential to determine the importance of the chancre to the early pathogenesis of African trypanosomiasis when the interplay between the host's initial immune responses and trypanosomal variants could dictate the subsequent course of the disease.

Acknowledgments. The authors thank Messrs. D. Bovell, P. Belsoi, J. Kamau, S. B. Kutuza and Miss F. Dar for excellent technical assistance. We are grateful for Drs. Max Murray and W. I. Morrison for advice on this paper. This is ILRAD publication No. 118.

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