

CIRCULATING LANGERHANS CELLS IN A DERMAL VESSEL

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Abstract. Langerhans cells were found within the lumen of a dermal vessel in a guinea pig. This vessel had the ultrastructural features of a lymphatic, and was at the site of a contact-allergic reaction to 2,4-dinitro-1-chlorobenzene (DNCB) to which the guinea pig had been passively sensitized by injection of peritoneal exudate and lymph node cells from strongly DNCB-sensitized donor guinea pigs. The significance of this finding remains to be determined.

Langerhans cells have been previously described near to but, to our knowledge, never within, dermal vessels (3, 7). While doing passive transfer studies of contact allergy in guinea pigs, we noted and herein report, Langerhans cells in the lumen of a dermal vessel.

MATERIALS AND METHODS

Six Hartley-strain male guinea pigs weighing between 400 and 600 g were sensitized to 2,4 dinitro-1-chlorobenzene (DNCB) by the technique of Maguire & Chase (9). Strongly sensitized (3+ to 4+) animals were used as donors for passive transfer tests (1). In each of three separate passive transfers, between 5×10^6 and 1×10^8 peritoneal exudate, lymph node, or spleen cells from 2 donor animals were pooled and injected into a single recipient animal. Two days after the cell transfer, 0.3% DNCB in olive oil was topically applied to a clipped skin site on the recipient animals. Skin reactions were read 24 hours later.

Skin biopsies were obtained from the recipient guinea pigs before and at intervals after application of DNCB 0.3% in olive oil. The specimens were processed for electron microscopy as reported elsewhere (12).

RESULTS

All recipient animals developed 1+ to 2+ reactions at the skin-test site. In one of 3 animals which had received peritoneal exudate cells intravenously and lymph node cells intraperitoneally,

Langerhans cells were seen by electron microscopy in the lumen of a superficial vessel in the dermis. This occurred at a site 48 hours after topical application of 0.3% DNCB i.e. 4 days after passive transfer of cells. Fig. 1 shows part of the lumen of a vessel containing two Langerhans cells and three mononuclear cells which morphologically resemble lymphocytes. Four endothelial cells are evident but no red blood cells, are seen. A basement membrane is present beneath the endothelium. This vessel resembles a lymphatic vessel (2). Fig. 2 shows a high-power view of one of these Langerhans cells and a lymphocyte-like cell. Fig. 3 shows the other Langerhans cell also at high magnification.

Langerhans cells were found in the dermis in all 3 recipient animals both before and after passive transfer. However, they appeared to be more numerous at DNCB-reactive sites, often appearing in groups of two or more near dermal vessels. Further details of the ultrastructural findings at the sites of passively-induced, contact-allergic reactions to DNCB will be reported elsewhere.

DISCUSSION

Langerhans cells were originally described in the epidermis, but have been found in other tissues, e.g. in the thymus (5, 10) and lymph nodes (4, 6, 8). Cells containing Langerhans granules have also been reported in monocytic leukemia (11). Wolf (13) has therefore stressed that the term Langerhans cell no longer exclusively denotes an intra-epidermal cell. He suggests that the available evidence indicates that the Langerhans granule is specific for a uniform cell line, no matter where these cells are encountered. To our knowledge,

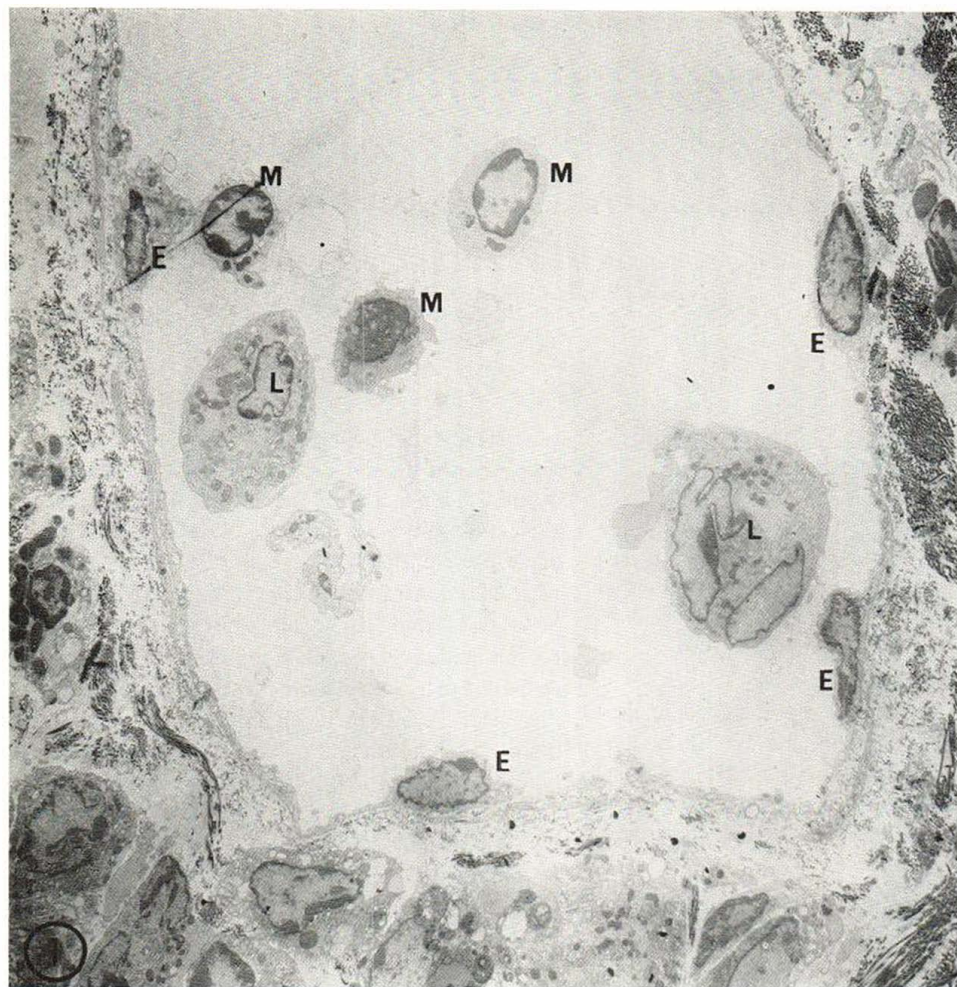


Fig. 1. Part of the lumen of a vessel containing two Langerhans cells (*L*) and three mononuclear cells (*M*) which morphologically resemble lymphocytes. No red

blood cells are seen. Four endothelial cells (*E*) are present. This vessel resembles a lymphatic. Stained with uranyl acetate and lead citrate, $\times 2\,500$.

Langerhans cell have not previously been reported in dermal vessels. The vessel in which they were observed by us is probably a lymph vessel, because of its morphologic characteristics and the absence of erythrocytes.

There are two possible sources for the circulating Langerhans cells which we found. The first is that they are derived from the passively-transferred, peritoneal exudate and lymph node cells, i.e., that they are cells from the donor guinea pig. The other is that they are derived from a tissue of the recipient guinea pig. It is not possible from our observations to determine in which

direction the Langerhans cells were travelling. However, it is obvious that Langerhans cells may find their way into the circulatory system. Whether or not the finding of Langerhans cells within a dermal lymph vessel is an exceptional occurrence requires further study.

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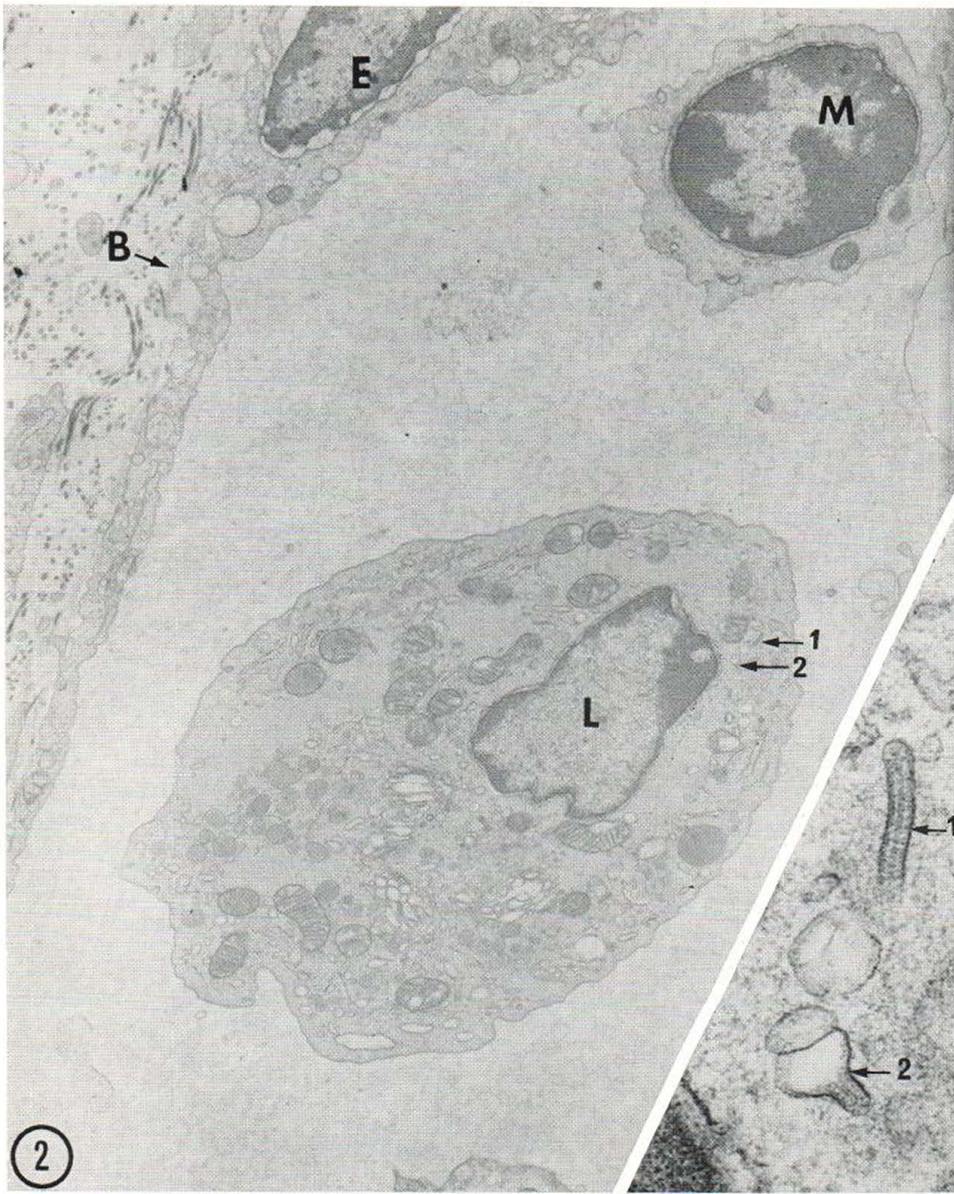


Fig. 2. High-power view of one of the Langerhans cells (L) shown in Fig. 1. The arrows (marked 1 and 2) indicate the locations of Langerhans granules. A lymphocyte-like cell (M) and part of an endothelial cell (E) are also

seen. The basement membrane (B) is thin and irregularly broken up, $\times 10\,500$. Langerhans granules are shown at higher magnification in the inset, $\times 91\,500$. Stained with uranyl acetate and lead citrate.

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REFERENCES

1. Baer, R. L. & Rosenthal, S. A.: Induction of cross tolerance for contact sensitivity by a non-immunogenic chemical. Feeding dichloronitrobenzene induces tolerance to dinitrochlorobenzene. *J Immunol* 108: 706, 1972.
2. Casley-Smith, J. R. & Florcy, H. W.: The structure of normal small lymphatics. *Q J Exp Physiol* 46: 101, 1961.
3. Ebner, H. & Niebauer, G.: Über den Nachweis von Langerhanszell-Organellen ausserhalb der Epidermis. *Klin Wochenschr* 79: 686, 1967.
4. Gianotti, F., Caputo, R. & Ranzi, T.: Ultrastructural study of giant cells and "Langerhans cell granules" in cutaneous lesions and lymph node and liver biopsies from four cases of subacute disseminated histiocytosis of Letterer-Siwe. *Arch Klin Exp Derm* 233: 238, 1968.

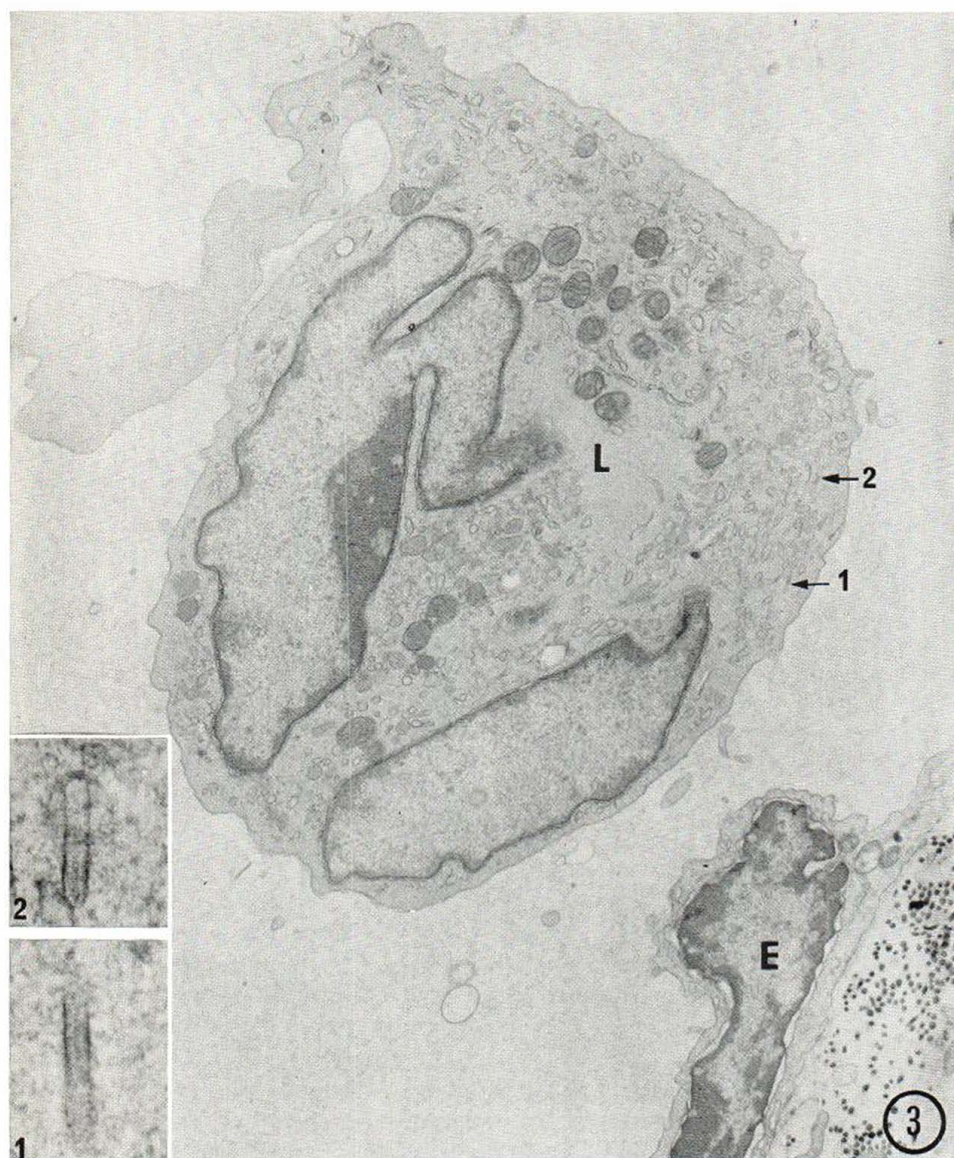


Fig. 3. The other Langerhans cell (L) which was shown in Fig. 1. The arrows (marked 1 and 2) indicate the positions of the Langerhans granules. Part of an endothelial

cell (E) is seen, $\times 10\,500$. The Langerhans granules are shown at higher magnification in the inset, $\times 91\,500$. Stained with uranyl acetate and lead citrate.

5. van Haelst, U. J.: Light and electron microscopic study of the normal and pathological thymus of the rat. III. A mesenchymal histiocytic type of cell. *Z Zellforsch* 99: 198, 1969.
6. Jimbow, K., Sato, S. & Kukita, A.: Cells containing Langerhans granules in human lymph nodes of dermatopathic lymphadenopathy. *J Invest Dermatol* 53: 295, 1969.
7. Kiistala, U. & Mustakallio, K. K.: The presence of Langerhans cells in human dermis with special ref-

- erence to their potential mesenchymal origin. *Acta Dermatovenere (Stockholm)* 48: 115, 1968.
8. Kondo, Y.: Macrophages containing Langerhans cell granules in normal lymph nodes of the rabbit. *Z Zellforsch* 98: 506, 1969.
9. Maguire, H. C., Jr & Chase, M. W.: Exaggerated delayed-type hypersensitivity to simple chemical allergens in the guinea pig. *J Invest Dermatol* 49: 460, 1967.
10. Olah, I., Dunay, C., Röhlich, P. & Törö, I.: A

- special type of cells in the medulla of the rat thymus. *Acta Biol Acad Sci Hung* 19: 97, 1968.
11. Sanel, F. T. & Serpick, A. A.: Plasmalemmal and subsurface complexes in human leukemic cells: membrane bonding by zipper-like junctions. *Science* 168: 1458, 1970.
 12. Silberberg, I.: Apposition of mononuclear cells to Langerhans cells in contact allergic reactions. *Acta Dermatovener (Stockholm)* 53: 1, 1973.
 13. Wolff, K.: The Langerhans cell. *Current Problems in Dermatology*, Vol. 4, pp. 79-145. Karger, Basel, 1972.

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