

or with blood previously passed through a pig liver⁵. Pig endothelium incubated with fresh dog serum showed changes within 15 min in each of four experiments with different endothelial lines, and the monolayer was completely disrupted within 90 min. The first change is that the endothelial cells become more rounded, and draw away from each other so that the cement lines after silver staining, which indicate close intercellular apposition, can no longer be demonstrated. The cells appear granular and vacuolated; many of them extrude cytoplasm as 'ghost bubbles'. At 90 min most of the cells have detached from the substrate and floated away. (Fig. 1b).

The damaged cells become 'sticky' to platelets—resuspended cells treated with dog serum and then mixed with

a dog platelet suspension become surrounded by platelets (Fig. 1c). Dog serum contains a heterophil antibody which agglutinates pig red cells and will cause their lysis in the presence of complement¹. Adsorption of dog serum with pig red cells at 4° C renders it innocuous to pig endothelium, and pig endothelial cells incubated with heat inactivated dog serum will form cross agglutination rosettes with pig red cells.

Exactly comparable effects can be produced by incubating pig endothelium with 'lymphocytotoxic' alloantisera and then treating it with rabbit serum as a complement source (pig serum is also effective, but some samples are 'anti-complementary'). In five experiments with different endothelial lines, changes were observed after 30 min and were marked at 60 min. Sera toxic to lymphocytes from a given pig were in each case toxic to endothelium from the same pig, but antisera to other specificities, pooled normal serum and specific antibody in the absence of complement were not. The damaged cells were again 'sticky' to pig platelets (these were obtained from pigs compatible with the antiserum used, to avoid the possibility of cross agglutination). The platelet-endothelial cell aggregates are similar to those described by Rafelson *et al.* after treatment of platelet-endothelial cell mixtures with thrombin⁶, and may be related to the platelet thrombi observed *in vivo*.

Similar effects on human endothelium have been observed as a result of treatment with antibodies to HL-A antigens (D. de B. and V. Joysey, in preparation).

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¹ Kissmeyer Nielsen, F., Olsen, S., Petersen, V. P., and Fjeldborg, V., *Lancet* **ii**, 662-665 (1966).

² Perper, R. J., and Najarian, J. S., *Transplantation*, **4**, 377-388 (1966).

³ White, D. J. G., Bradley, B., Calne, R. Y., and Binns, R. M., *Transpln Proc.*, **V**, 317-320 (1973).

⁴ Jaffe, E. A., Nachman, R. L., Becker, C. G., and Minick, C. R., *J. clin. Invest.*, **52**, 2745-2756 (1973).

⁵ Rafelson, M., Hoveke, T., and Booyse, F. M., *Ser. Haemat.*, **VI**, 4, 367-374 (1973).

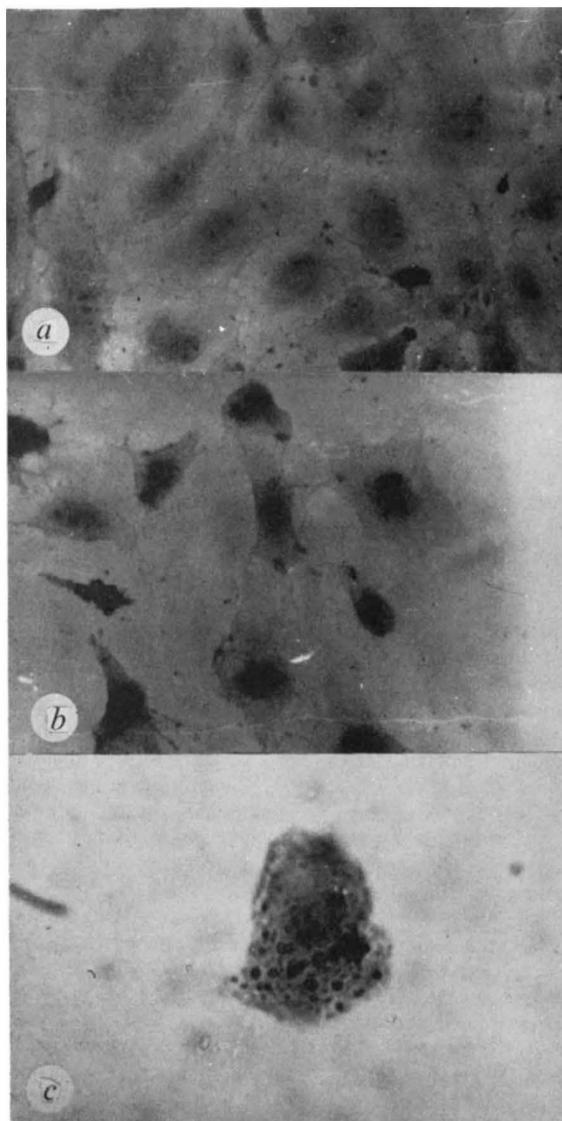


Fig. 1 *a*, Monolayer of normal pig endothelium in culture, stained silver and haematoxylin; *b*, pig endothelium treated for 30 min with 'lymphocytotoxic' antiserum, then for 35 min with baby rabbit serum; *c*, pig endothelial cell surrounded by platelets. About 75,000 resuspended endothelial cells were spun down and treated with 50 μ l of specific pig anti-PLA serum for 30 min, washed, treated with 100 μ l rabbit serum for 30 min and added to 0.5 ml of pig platelet suspension. The mixture was gently shaken for 5 min in a siliconed tube. Smears were made and stained with Giemsa.

Erratum

In the article "Thegosis in herbivorous dinosaurs" by R. A. Thulborn (*Nature*, **250**, 729; 1974) the seventh line in para 4 should read 'facets usually occur towards the cervix at the anterior or' . . . and not as printed.

In the article "TRH potentiates behavioural changes following increased brain 5-hydroxytryptamine accumulation in rats" by A. R. Green and D. G. Grahame-Smith (*Nature*, **251**, 524; 1974) Figs 1 and 2 were transposed over their appropriate legends.

In the article "B and T-cell stimulatory activities of multiple mitogens from pokeweed" by M. J. Waxdal and T. Y. Basham (*Nature*, **251**, 163; 1974) Figs 2 and 3 have been interchanged. The legends are correct as they stand.