single selected dose of 10 (μg/kg)/min into the descending aorta superior to the origin of the superior mesenteric artery. These effects were not modified by hexamethonium bromide (1·0–5·0 mg/kg, I.V.).

Larger doses of histamine (up to 40 (μg/kg)/min, I.V.) irregularly produced rises in C.F.C., indicative of a dilatation of the precapillary sphincters, and similar rises could be produced regularly with the lower doses of histamine (0·01–10·0 (μg/kg)/min) after the administration of the α-adrenoceptor blocker phentolamine mesylate (1·0 mg/kg, I.V.) or after aminoguanidine bicarbonate (10 mg/kg, I.V.), a drug which inhibits histaminase activity and hence enhances the effects of exogenous histamine (Ghosh & Schild, 1958).

Mepyramine maleate (1·0 mg/kg, I.V.) blocked both the increases and the decreases in C.F.C. that resulted from histamine.

Histamine has been implicated in the release of catecholamines from the chick intestine *in vitro* (Everett & Mann, 1967), and, in doses comparable to those used in the present study, from the suprarenal glands of cats and dogs (Staszewska-Barczak & Vane, 1965), and it seems possible that the present results might be related to this phenomenon.

Schayer (1962) produced evidence to suggest that locally produced histamine has a role as an 'intrinsic regulator' of the microcirculation. The results of the present investigation show that exogenous histamine has profound and partially unexpected effects on the intestinal microcirculation, but do not in themselves suggest a physiological role of histamine in this tissue. Compound 48/80 (100 μg/kg, I.V.), which releases histamine from mast cells, causes a biphasic response of a large transient increase in C.F.C. followed by a sustained fall.

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Biochemical and cellular changes in the Arthus reaction

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New Zealand White rabbits were immunized with alum-precipitated ovalbumin (1 mg S.C. and 0·5 mg I.V.) and 4 weeks later were challenged with intradermal injections of 1 mg ovalbumin into the lower hind limb to induce an Arthus reaction. Changes were studied in the Arthus site and in the afferent lymph draining the site before it entered the popliteal node.

Erythema and oedema were established at the Arthus site 2–4 h after challenge although the intensity of erythema continued to increase up to 24 h. During this time there was a gradually increasing infiltration of leucocytes, mainly consisting of polymorphonuclear cells with some eosinophils and monocytic cells.

At the Arthus site there was a significant increase in protein concentration from 2 h onwards. There was also an increase in the activities of lactic dehydrogenase (LDH), β-glucuronidase (β-gluc), cathepsin D and glutamic oxalacetic transaminase (GOT). These increases were significant at 4 h and again between 12 and 36 h after challenge. However, there was no consistent increase in the activities of acid phosphatase or glutamic pyruvic transaminase.

In the lymph there was no increase in the protein concentration, which must therefore have been retained at the Arthus site. This retention does not occur after a non-immunological inflammatory reaction such as thermal injury in which the plasma protein passes directly into the lymph.

In the lymph pellet (i.e., leucocytes separated by centrifugation) there was an increase starting 4–8 h and reaching a maximum 16–20 h after challenge, in the activities of LDH, β-gluc, cathepsin D and GOT. This increase corresponded to the increasing number of cells leaving the site of injury and entering the lymph.

In the lymph supernatant there was an increase only in LDH, β-gluc and GOT at 16–20 h. At least part of the β-gluc probably originated in the plasma where there is a high level of this enzyme. There was no increase in the activity of cathepsin D in the supernatant although it was increased in the pellet and at the Arthus site. Therefore if the LDH and GOT (and possibly part of the β-gluc) activities originated at the Arthus site from damaged cells it must be postulated that cathepsin D was inactivated in some way. On the other hand, if they originated in leucocytes which had left the site and entered the lymph, it seems likely that there was leakage only of cytoplasmic enzymes and not of lysosomal enzymes.

A new approach for studying the influence of cyclophosphamide upon the rejection of rabbit skin homografts

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Previously, Bitterli & Jasani (1972) showed that during the homograft reaction changes in dry weight parallel increases in vascularity of the graft, increases in the moisture content reflect changes in vascular permeability and those in the DNA content indicate increases in the cellularity of the graft.

The present experiments show that when the homograft reaction is suppressed the changes of these three parameters are modified such that they resemble the corresponding changes in skin autografts.

When the rabbits received daily intravenous injections of cyclophosphamide, so that the total dose was 745 mg per animal, the reaction was maximally suppressed. In these experiments the tissue dry weight and DNA of the homografts did not increase above the values found in autografts that were transplanted onto similar anatomical sites in the opposite leg of the same animal, and which therefore constituted the internal control. The two types of graft, i.e., homografts and autografts in these animals, also resembled each other in outward appearance and histologically in both epithelial hyperplasia was present and lymphocytic mononuclear cells virtually absent.

In contrast, in rabbits receiving a total dose of cyclophosphamide of 445 mg/animal, rejection was only partially suppressed, i.e., the healthy pink appearance of their homografts did not last for even as long as 24 h beyond the expected time of onset of rejection. Whilst their autografts continued to be incorporated normally into the surrounding skin, the homografts of these animals became bluish purple and firm in consistency, and histologically they developed evidence of mononuclear cell infiltration. In this group the DNA as well as the dry weight of homografts increased to a significantly greater extent than in the paired autografts. However, although the influence of this dose of cyclophosphamide was not detectable using the usual three parameters, there were differences in the histological changes in the grafts. Compared with homografts of the non-treated animals, the degree of epithelial hyperplasia was greater whereas the mononuclear cells were fewer.

Although the estimation of DNA provides an accurate assessment of cellularity, it does not give an indication of changes in the population of different cell types.

Therefore new parameters were necessary to distinguish between hyperplasia of cells normally present in the skin and changes in the number of migratory cells. Earlier