When tranylcypromine (10^{-6}—10^{-5}M), a monoamine oxidase inhibitor that does block uptake, was used, both inhibition of removal of 5-HT by the lung and prolongation of the contractions of the rat stomach strips were seen.

These experiments were repeated using ^{3}H-5-HT and the total radioactivity, ^{3}H-5-HT and ^{3}H-metabolites appearing in the perfusate determined. There was good correlation between the amounts of biologically-active 5-HT and radioactive 5-HT in the perfusate.

We conclude that the infused 5-HT is not taken up and stored in the lungs in structures analogous to the granules in platelets or rat mast cells, because 5-HT in these storage sites is protected from enzymic inactivation. However, the initial uptake process does show similarities to amine uptake in platelets or nerve endings in that it is inhibited by amitriptyline, desmethylimipramine or tranylcypromine.

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REFERENCES

AXELROD, J. & INSCOE, J. K. (1963). The uptake and binding of circulating serotonin and the effect of drugs. *J. Pharmac. exp. Ther.*, **141**, 161–165.

GADDUM, J. H., HEBB, C. O., SILVER, ANN & SWAN, A. A. B. (1953). 5-Hydroxytryptamine: Pharmacological action and destruction in perfused lung. *Q. Jl exp. Physiol.*, **38**, 255–262.

IVERSEN, L. L. (1965). Inhibition of noradrenaline uptake by drugs. *J. Pharm. Pharmac.*, **17**, 62–64.

THOMAS, D. P. & VANE, J. R. (1967). 5-Hydroxytryptamine in the circulation of the dog. *Nature, Lond.*, **216**, 335–338.

VANE, J. R. (1957). A sensitive method for the assay of 5-hydroxytryptamine. *Br. J. Pharmac. Chemother.*, **12**, 344–349.

Intracellular enzymes in local lymph after chemical injury.

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It was shown earlier in cats (Lewis, 1967) and rabbits (Lewis, 1969) that after thermal injury the extent of cellular damage could be assessed by estimation of the increase in concentrations of various intracellular enzymes escaping from the injured tissue into the local lymph.

The purpose of the present investigation was to determine if the effects of chemical injury could be assessed in the same way. Dimethyl sulphoxide (DMSO) and croton oil were selected to produce mild and strong tissue injuries respectively.

Cats and rabbits were anaesthetized with pentobarbitone sodium (40 mg/kg) and lymph was collected via a polythene cannula inserted into the main femoral lymphatic as described by Lewis & Westcott (1968). After collecting a control sample of lymph, six subcutaneous injections of 0·2 ml DMSO or croton oil undiluted or diluted with corn oil were made at different sites in the hind leg. Lymph was collected continuously for a further 4–6 hr.

The concentrations in the lymph and plasma of protein potassium and six enzymes representing different intracellular compartments were estimated. The methods used were those quoted in the earlier papers and the enzyme localization was after Hess (1963).

Injection of DMSO caused an increased concentration in the hind limb lymph of the cytoplasmic enzymes lactic dehydrogenase and glutamic oxalacetic transaminase in cats and rabbits, and an increase in the mitochondrial enzyme glutamic pyruvic transaminase in rabbits. The concentration of the lysosomal enzymes acid phosphatase and cathepsin did not increase in the cat or rabbit lymph. This pattern of intracellular enzymes in the lymph was similar to that produced by a 60°C superficial burn, but the effect on protein concentration was different. After thermal injury, the protein invariably increased together with the lymph flow. But after DMSO, although there was a considerable increase in lymph flow, the protein fell significantly.

Injection of undiluted croton oil caused leakage of all enzymes including those from lysosomes, as well as protein and K^+ in both species. This pattern of enzymes in the lymph indicates a strong injury with cell necrosis and is comparable with that produced when the limb was frozen, causing cell break-down.

In rabbits, 50 and 75% croton oil in corn oil caused a less severe injury; all the enzymes were released, but to a lesser extent. This indicates that, like neat croton oil, the diluted solutions cause cell necrosis but affect a smaller number of cells. This is in contrast to the effect of DMSO, where the enzyme pattern indicated that as many cells were affected as with croton oil, but instead of causing cell necrosis, DMSO caused a change which allowed the escape of selected enzymes.

Histological findings were consistent with this view since, whereas after DMSO there was evidence of only vasodilatation and occasional oedema, there was gross oedema with obvious cell necrosis after croton oil.

REFERENCES

HESS, B. (1963). *Enzymes in Blood Plasma*, p. 7. New York and London: Academic Press.
LEWIS, G. P. (1967). Intracellular enzymes in local lymph as a measure of cellular injury. *J. Physiol., Lond.*, **191**, 591–607.
LEWIS, G. P. (1969). The composition of rabbit hind limb lymph after thermal injury. *J. Physiol., Lond.*, **205**, in the Press.
LEWIS, G. P. & WESTCOTT, BARBARA (1968). Intracellular enzymes in rabbit hind limb lymph after injury. *J. Physiol., Lond.*, **195**, 12–13*P*.

Turnover of pulmonary alveolar wall cells in guinea-pig and mouse after anaphylactic shock.

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Experimentally induced anaphylaxis produces a different response in guinea-pig and mouse. In guinea-pig the critical organ is the lung and acute respiratory distress due to bronchiolar constriction is brought about by release within the lung of histamine, 5-hydroxytryptamine (Sanyal & West, 1958) and slow reacting substance in anaphylaxis (SRS-A) (Brocklehurst, 1953, 1955, 1960). In mouse a generalized systemic shock is observed, thought to be due to 5-hydroxytryptamine, released from enterochromaffin cells of the gastrointestinal tract.

Guinea-pigs surviving severe shock appear to recover within 24 hr, but histological studies have shown that extensive haemorrhage and pulmonary oedema are commonly found in such animals. Areas of irreversible damage consolidate and connective tissue scar formation occurs. The fate of pulmonary alveolar wall cells in areas where