Tissue histamine and catecholamines in the reparative process

SIR,—Histamine is recognized as one of the chemical mediators in the process of inflammation (Bhatt & Sanyal, 1964; Schayer, 1964).

It has recently been suggested (Spector & Willoughby, 1964) that the inflammatory changes following injury may be due to local inactivation of endogenous anti-inflammatory substances, like catecholamines. In the rat there is a reduction in the level of catecholamines in the injured skin (Moller, 1962) with a rise in the monoamine oxidase activity (Raekallio, 1963). When monoamine oxidase inhibitors are used, there is a striking diminution in the increased permeability caused by an injurious stimulus. This has lent further support to the above view (Spector & Willoughby, 1964).

The relevant studies, so far, have been made during the exudative phase of inflammation. The present experiments were undertaken to assess the relative roles played by histamine and by catecholamines in the reparative phase in the rat.

The skin histamine was depleted by repeated injections of polymyxin B (Parratt & West, 1957). The catecholamine metabolism was blocked by monoamine oxidase inhibitors, like nialamide or iproniazid; and catechol-*O*-methyl transferase inhibitors, like pyrogallol or quercitin. The quantity of the granulation tissue developed under various experimental circumstances was measured by the cotton pellet method (Finney & Somers, 1958). The strength of the fibres was assessed by measuring the tensile strength of the scar tissue (Fenton & West, 1963). The animals were killed for various estimations 10 days after producing injury.

In the polymyxin B treated animals there was a marked reduction in the tensile strength with only a slight reduction in the granulation tissue. The tensile strength of the scar tissue was also reduced in animals treated with monoamine oxidase inhibitors though the total amount of the granulation tissue was little affected.

In animals treated with pyrogallol, the amount of the granulation tissue as well as the tensile strength were reduced. A large reduction in the tensile strength but not in the granulation tissue, was seen in the rats treated with quercitin.

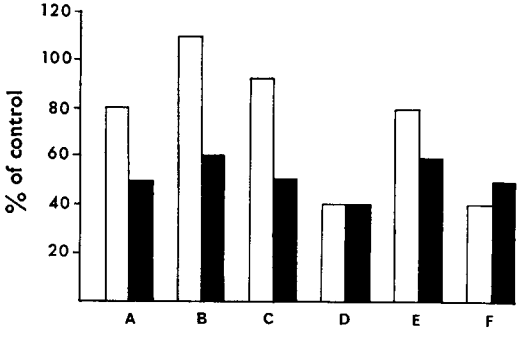

FIG. 1. The effect of various drugs on the granulation tissue formation (open columns) and tensile strength (solid columns) of scar tissue in the rat. A. Polymyxin B, 5 mg/kg. B. Nialamide, 80 mg/kg. C. Iproniazid, 40 mg/kg. D. Pyrogallol, 200 mg/kg. E. Quercetin, 50 mg/kg. F. Betamethasone, 2·5 mg/kg. Drugs were injected intraperitoneally daily for 10 days.

When the animals were treated with a potent anti-inflammatory corticosteroid such as betamethasone, the total amount of granulation tissue as well as the tensile strength were much reduced. The results are illustrated in Fig. 1.

It was thus seen that the processes which either lead to a reduction in the tissue histamine content or which block the pathway of catecholamine disposal, affect the reparative process in such a way as to produce a poor quality of granulation tissue without markedly affecting the total quantity.

Since both histamine and catecholamines take part in the early exudative phase as well as in the late reparative process, it is possible that a dynamic balance between these two biogenic amines may be one of the factors determining the ultimate inflammatory response of the tissues.

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