In recent years, the search for new topical corticosteroids has been generally focused on the potency of action and based on tests which set in evidence the vascular component of inflammation, such as cutaneous vasoconstriction, skin stripping, irritant induced erythema, etc. (1-4). Since steroid-responsive dermatoses include disorders in which the predominant reaction is either vascular (e.g. acute eczema, contact dermatitis) or cellular (e.g. chronic eczema, dry eczema), we compared the effects of three different corticosteroids on both the vascular and cellular components of inflammation in some common laboratory tests.

Betamethasone, a fluorinated corticosteroid, hydrocortisone, a non fluorinated corticosteroid and the hydrocortisone-bendazac ester were studied, the latter being included in the study on account of its unusual spectrum of activity (5). Carrageenin paw edema and cotton pellet granuloma were used as inflammatory responses; the former represents a model in which the vascular component prevails, the latter a model in which cellular proliferation prevails.

Long Evans rats of both sexes, weighing 150-180 g, were used. The animals were given a standard diet and water ad libitum. Betamethasone valerate, hydrocortisone acetate and the hydrocortisone-bendazac ester were used. The carrageenin paw edema was induced according to the method Winter et al. (6). The paw was measured 2 hr after injection of the drugs suspended in carrageenin (0.05 ml of a 1% solution). The cotton pellet granuloma test was performed according to the method of Meier et al. (7). Two sterile cotton pellets were symmetrically implanted into the back of each rat. One pellet was soaked with 0.5 ml of an ethanol solution of the products, the other with the solvent alone. Before implantation, the pellets were dried (40°C for 24 hr). Three days later, the animals were sacrificed and the granulomata removed, dried (60°C for 24 hr) and weighed. Since the regression curves were not parallel, the potency ratios for each drug in the carrageenin and cotton pellet tests were calculated on the basis of the minimal effective concentration (MEC).

The effects of various concentrations of betamethasone, hydrocortisone and hydrocortisone-bendazac ester on carrageenin paw edema are reported in Figure 1. All drugs

1) Data presented at the Joint Meeting of German and Italian Pharmacologists, Venice, October (1977)
under study inhibit this type of inflammatory response, the degree of inhibition being dependent on the concentration used. The minimal effective concentrations are as follows: betamethasone 0.01 mg%, hydrocortisone 0.6 mg% and hydrocortisone-bendazac ester 0.5 mg%.

The effects of various concentrations of betamethasone, hydrocortisone and hydrocortisone-bendazac ester on cotton pellet granuloma are shown in Fig. 2. All the drugs show a concentration related anti-granuloma activity. The minimal effective concentrations are 0.4 mg% for betamethasone, 12.5 mg% for hydrocortisone and 5.0 mg% for hydrocortisone-bendazac ester.

The results of these experiments show that in the carrageenin test, a model of inflammation in which the vascular component prevails, betamethasone is 60 times more active than hydrocortisone and 50 times more active than hydrocortisone-bendazac ester. In the granuloma test, in which cellular proliferation prevails, betamethasone is only 31 times more potent than hydrocortisone and 12 times more potent than the hydrocortisone-bendazac ester. Thus, the vascular and cellular effects of the corticosteroids are not in parallel; consequently, their spectrum of activity differs. A comparison of the minimal effective concentration in the carrageenin and granuloma tests shows that betamethasone is the most specific drug as far as vascular activity is concerned (40 times more active in the carrageenin
than in the granuloma test), followed by hydrocortisone (20 times more active in the carrageenin than in the granuloma test), while hydrocortisone-bendazac ester is the least specific drug, with a potency ratio for the two activities of only 10:1.

As the effects of topical application of a drug in the form of ointment may differ from those seen with injection, our results suggest that in the therapeutic use of topical corticosteroids, not only their potency, but also the spectrum of anti-inflammatory activity should be taken into consideration. Fluorinated corticosteroids, like betamethasone, should be used in acute inflammatory conditions of the skin, where the vascular component prevails. On the other hand, non-fluorinated corticosteroids, such as hydrocortisone and hydrocortisone-bendazac ester, should be given preference in chronic conditions where cellular proliferation prevails.

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DECREASE IN PAIN THRESHOLD IN SART STRESSED MICE

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We have turned our attention to the so-called vegetative “Stigmatisierte” occurring in early spring or early autumn when there is a rapid change in temperature within one day, and we attempted to induce these states in experimental animals. When mice and rats had been reared under the conditions of alternating rhythm in temperature from 24°C to 8°C (or −3°C), all animals displayed symptoms usually seen with disturbances in the autonomic nervous system. The abnormal state is termed “SART stress” (specific stress state caused