

Effect of formaldehyde-induced peri-arthritis upon the composition of cotton-pellet granuloma in rats

SIR,—It is known that a local inflammatory reaction can be inhibited by prophylactic counter irritation. Laden, Blackwell & Fosdick (1958) found that injection of an irritant into the knee of a rat reduced the experimental pleuritis in the same animal. Intraperitoneal injection of substances that induce inflammatory oedema also inhibit the local inflammation of the rat paw (Büch & Wagner-Jauregg, 1962; Benitz & Hall, 1963; Horáková, 1964). The local necrosis of the rat skin elicited the loss of dermal-insoluble collagen in apparently uninjured skin distal to the site of injury. The changes were similar to those in the necrotic area (Houck, 1962). We have now examined the influence of formaldehyde-induced peri-arthritis of the hind paw on the composition of experimental cotton-pellet granuloma in rats.

Experimental peri-arthritis of the right hind paw was produced in Wistar rats, of 150 g, by the injection of 0.2 ml of 2% formaldehyde under the plantar aponeurosis. Three days after this injection, two sterile cotton-pellets weighing 10 mg each were implanted under the skin of the back. After 7 and 21 days the induced granulomas were dissected, the pellets removed, and the tissue dried at 105° for 20 hr and then weighed. The dry tissue was analysed for its content of hydroxyproline, which was used as an indicator of fibrillar proteins (Stegemann, 1958) and also for the content of deoxyribonucleic acid (Schneider, 1945). The inflammation of the paw showed a typical course towards a chronic fibro-productive phase, with occasional necrosis. The results were compared with a control group without experimental peri-arthritis.

TABLE 1. DRY WEIGHTS OF GRANULOMAS AND THEIR HYDROXYPROLINE AND DEOXYRIBONUCLEIC ACID CONTENTS

		Dry weight of granulomas, mg	Hydroxyproline, $\mu\text{g}/100\text{ mg dry wt}$	DNA, $\mu\text{g}/100\text{ mg dry wt}$
7 Days	Controls	39.41 ± 9.10	1354.5 ± 134.8	1840.5 ± 356.0
	Formaldehyde peri-arthritis	40.34 ± 11.16	1933.3* ± 247.1	1991.4 ± 219.2
21 Days	Controls	35.11 ± 9.32	1332.9 ± 382.9	2047.6 ± 339.9
	Formaldehyde peri-arthritis ..	37.29 ± 13.29	1747.8* ± 396.7	3062.1* ± 280.9

* Statistically significant difference $P < 0.02$.

Table 1 shows that the weights of the dried granulomas were not different in the group with formaldehyde-induced peri-arthritis compared with the control group. The contents of hydroxyproline and deoxyribonucleic acid, on the other hand, were changed. There was elevation of the hydroxyproline content on the 7th and 21st day of the experiment and the deoxyribonucleic acid level elevated significantly on the 21st day. The local injury of the hind paw may thus be paralleled, according to these biochemical indicators, by an enhanced fibroproliferative reaction in the cotton-pellet granuloma. This is different to the oedematous reactions. Whether this is a result of a change in the reactivity of the connective tissue in general remains to be proved.

The technical assistance of E. Dobošová and V. Lapárová is gratefully acknowledged.

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February 9, 1965

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The nature of the inhibition of the rat uterus by relaxin

SIR,—Wiqvist (1959) presented evidence that the inhibitory action of relaxin on the spontaneous contractions of the isolated uterus of the rat was not blocked either by phentolamine or by dihydroergotamine in concentrations which blocked the inhibition of the these contractions by adrenaline. He suggested that relaxin acted otherwise than by the adrenergic mechanism suggested by Miller & Murray (1959). However, a fuller investigation of these actions by Rudzik & Miller (1962a, b) added weight to their original contention that the mechanism was

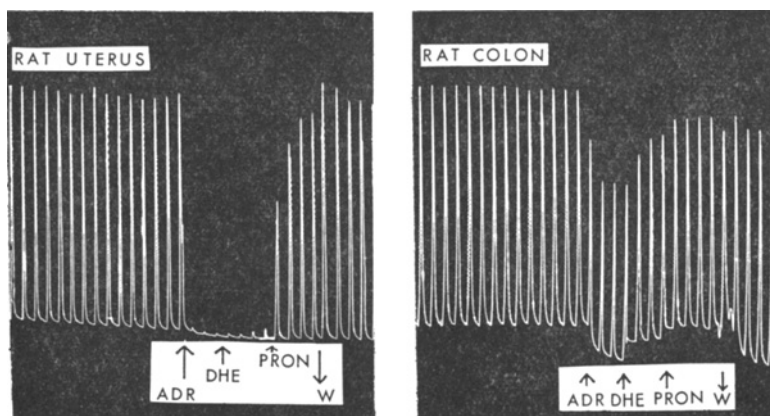


FIG. 1. Effects of pronethalol and dihydroergotamine on inhibitory actions of adrenaline. Isotonic contractions of the electrically stimulated rat uterus. At ADR 5×10^{-9} (-)-adrenaline, at DHE 5×10^{-7} dihydroergotamine and at PRON 5×10^{-7} pronethalol were added to the bath. The drugs were washed out at W. Isotonic contractions of the electrically stimulated rat colon. Legend as for uterus except for ADR, where 5×10^{-8} (-)-adrenaline was added to the bath.

adrenergic. The blocking drugs used by both groups, dihydroergotamine and phentolamine caused adrenergic block at α -receptors, but are now recognised to lack specificity (Ahlquist & Levy, 1961; Birmingham & Wilson, 1963). Also, the action of adrenaline on the rat uterus is known to be almost entirely at β -receptors (Levy & Tozzi, 1963; Levy, 1964). With the advent of a β -receptor blocking agent of high specificity, pronethalol (nethalide) (Black & Stephenson,