lins, Cryer, Inch & McLaughlin, 1979) and the GABA transport inhibitors (±)-nipecotic acid (100 μM) and (±)-cis 3-aminocyclohexane carboxylic acid (100 μM) failed to reduce total binding.

Specific binding could be detected in fresh as well as frozen tissue provided that the pellet in both cases was pretreated with Triton-X-100 (cf. Enna & Snyder 1976).

We conclude that the saturable Na^+ independent binding of [^{3}H]-GABA and [^{3}H]-muscimol observed in these experiments is associated with the GABA receptor.

D.R.H. is an S.R.C. student.

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The actions of cimetidine, mepyramine, indomethacin and aprotinin (Trasylol) on the inflammatory response in adjuvant rats

H.A. AL-HABOUBI & I.J. ZEITLIN

Department of Physiology and Pharmacology, University of Strathclyde, George Street, Glasgow, G1 1XW, Scotland, U.K.

To study the relative importance of histamine, kinins and prostaglandins in the development of chronic inflammation, the effects of some inhibitors of the actions or formation of these mediators have been evaluated using rats with adjuvant arthritis.

Adjuvant arthritis was induced in male Wistar rats (350–450 g) by a single injection of Freund's complete adjuvant (0.1 ml) into the left hind paw (Newbould, 1963). The acute response was followed for the first 6 h by half-hourly measurement of percentage increase from zero time (D%) of left hind paw volumes, using a Basile differential volume meter. The chronic response was followed for 14 days by daily measurement of the D% of stifle joint lateral diameters using vernier callipers. Drugs were administered 2 h prior to adjuvant injections and thereafter at 24 h intervals. Control groups contained untreated adjuvant injected rats. Results are shown in Table 1.

In the untreated adjuvant controls, all paw volumes increased continuously throughout 6 hours. The mean D% in stifle joint diameters showed a biphasic pattern, peaking at day 4, decreasing until day 6 and increasing again to plateau between days 9–14.

Indomethacin, a cyclooxygenase inhibitor and Trasylol, an inhibitor of kallikrein and similar proteases, produced large reductions in the development of both acute and chronic responses. Thus, both arachidonate metabolites and kinin-forming enzymes or similar proteases were apparently involved in the development of both phases of inflammation. Mepyramine maleate, an H_1 antihistamine reduced the D% in joint diameter only between days 1–4, while cimetidine hydrochloride, an H_2 antagonist suppressed both the acute and chronic responses at all stages after 3 hours. The presence of H_2 but not H_1 receptors has been reported in the synovial vasculature in dogs (Grennan, Rooney, St. Onge, Brooks, Zeitlin & Dick, 1975).

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Table 1 Effects of indomethacin, aprotinin, mepyramine maleate and cimetidine-hydrochloride on the development of the acute and chronic phases of adjuvant arthritis

	Percentage increase (mean ± s.d.)†						
	Left paw volume			*Right stifle joint diameter*			
	3 h	*4.5 h*	*6 h*	*day (4)*	*day (6)*	*day (9)*	*day (14)*
Adjuvant	36.8 ± 10.3	67.8 ± 36.3	80.4 ± 25.7	17.0 ± 0.9	6.3 ± 2.7	17.5 ± 3.9	17.8 ± 2.0
Control	(6)	(6)	(6)	(12)	(12)	(12)	(12)
Indomethacin	13.3 ± 16.6	10.5 ± 10.1	10.9 ± 11.8	11.0 ± 1.6	1.8 ± 1.0	9.2 ± 3.7	10.9 ± 4.0
2.5 mg/kg (p.o.)	(5)*	(5)**	(5)**	(6)***	(6)*	(6)***	(6)*
Aprotinin	31.6 ± 13.7	24.1 ± 9.0	21.3 ± 4.8	8.1 ± 3.6	3.4 ± 1.6	9.7 ± 3.6	10.0 ± 4.0
2000 i.u./kg (i.v.)	(6)	(6)***	(6)***	(6)***	(6)	(6)***	(6)**
Mepyramine Maleate	24.1 ± 17.7	66.7 ± 32.8	48.1 ± 27.4	13.0 ± 1.8	6.0 ± 4.2	16.5 ± 3.3	18.4 ± 3.6
1 mg/kg (i.p.)	(6)	(6)	(6)	(6)**	(6)	(6)	(6)
Cimetidine-HCl	24.6 ± 20.3	26.1 ± 14.2	18.9 ± 12.6	7.5 ± 3.9	2.5 ± 0.8	8.9 ± 2.4	8.3 ± 2.6
1 mg/kg (i.p.)	(6)	(6)**	(6)***	(6)***	(6)**	(6)***	(6)***

† The numbers of observations are given in brackets. The acute and chronic inflammation values are derived from two separate experiments. Statistical significance of differences between test and control groups determined using Mann-Whitney U-test (one-tailed).
* $P \leqslant 0.05$; ** $P \leqslant 0.01$; *** $P \leqslant 0.001$.

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The effect of some anti-rheumatic agents on tuberculin pleurisy in the guinea-pig

A. BLACKHAM & AUDREY M. WOODS

Fisons Limited, Pharmaceutical Division, Research and Development Laboratories, Bakewell Road, Loughborough, Leicestershire. LE11 0QY

It seems likely that the inflammatory events inaugurated and perpetuated by the interaction of lymphocyte products and phagocytic cells cause some of the pathological lesions observed in rheumatoid arthritis (RA). The pleural cavity provides a discrete anatomical site where the temporal progression of cell-mediated delayed hypersensitivity reactions can be observed both qualitatively and quantitatively (Allen & Apicella, 1968). The volume of exudate and numbers of inflammatory cells (Leibowitz, Kennedy & Lessof, 1973; Yamamoto, Dunn, Capasso, Deporter & Willoughby, 1975) and the involvement of lymphokines (Yamamoto, Dunn & Willoughby, 1976) resulting from intrapleural injection of purified protein derivative (PPD) into guinea pigs previously sensitized with Freunds complete adjuvant (FCA) have been described elsewhere. Some of these parameters will be discussed further, together with a description of histochemical methods used to differentiate cell types and the biochemical estimation of the release of β-glucuronidase. The effect of representative drugs used in the treatment of RA on three parameters of tuberculin pleurisy in the guinea pig, viz: exudate volume, total cell count and β-glucuronidase release, has been assessed.

Guinea-pigs sensitized 4–5 weeks previously to FCA were challenged by intrapleural injection of PPD (1.25 μg). Forty-eight h later the animals were sacrificed and the pleural exudate volume and total and differential cell counts were measured. Diluted samples of cell free supernatant or cell lysate were used to measure β-glucuronidase as a marker of lysosomal enzyme release. Drugs were administered at the doses, times and routes shown in the table.

Steroids and gold salts reduced all three parameters. Indomethacin had little effect on exudate volume or cell infiltration but invariably increased β-glucuronidase release. Penicillamine on the other hand significantly reduced both exudate volume and