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).
* $P \leqslant 0.05$; ** $P \leqslant 0.01$; *** $P \leqslant 0.001$.

References

GRENNAN, D.M., ROONEY, P.J., ST. ONGE, R.A., BROOKS, P.M., ZEITLIN, I.J. & DICK, W.C. (1975). Histamine receptors in the synovial microcirculation. *Eur. J. clin. Invest.*, **5**, 75–82.

NEWBOULD, B.B. (1963). Chemotherapy of arthritis induced in rats by mycobacterial adjuvant. *Br. J. Pharmac.*, **21**, 127–136.

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

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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

Table 1 The effect of anti-rheumatic agents on three parameters of tuberculin pleurisy in the guinea-pig

Drug	Dose (mg/kg)	Route	Time* Schedule	% Changes Exudate Volume	% Changes Total Cell Count	% Changes β-glucuronidase Release
Prednisolone	40	Oral	A	−44.9†	−32.4†	−24.5
Myocrisin	2.5 (Au)	i.m.	B	−34.5	−25.4	−5.8
	5 (Au)	i.m.	B	−79.7†	−43.2†	−33.1
	10 (Au)	i.m.	B	−96.8†	−79.0†	−65.0†
Indomethacin	20	Oral	A	+4.7	+7.3	+43.9
Penicillamine	50	i.p.	B	−34.3	+4.7	−36.2†
	12.5	i.p.	C	−31.8	+7.3	−47.4
	25	i.p.	C	−53.3†	−11.3	−63.4†
	50	i.p.	C	−52.1†	−7.6	−67.5†
	100	i.p.	C	+14.6	+5.7	−29.6
Chloroquine	50	Oral	B	−5.5	−20.1	+40.0
	100	Oral	B	−19.9	−19.5	+4.2
Levamisole	5	Oral	B	−10.8	−30.9	−1.0
	15	Oral	B	−1.4	−17.8	−6.5
	45	Oral	B	−16.6	−2.1	−25.2
	50	Oral	B	+43.6	+14.4	+68.9

* Time Schedules: A = 1 h before and 24 h after challenge. B = 48, 24 and 1 h before and 24 h after challenge. C = Dosed 5/7 days per week for 5 weeks starting 6 days before sensitization.
† Significantly different from controls ($P < 0.05$) by Student's '*t*' test.

enzyme release without affecting the population of cells. This effect is best seen in animals which have been dosed over a long period. Chloroquine and levamisole produced inconsistent effects using the dosing regimens tried so far.

References

ALLEN, J.C., & APICELLA, M.A. (1968). Experimental pleural effusion as a manifestation of delayed hypersensitivity to tuberculin PPD. *J. Immunol.*, **101**, 481–487.

LEIBOWITZ, S., KENNEDY, L., & LESSOF, M.H. (1973). The tuberculin reaction in the pleural cavity and its suppression by anti-lymphocyte serum. *Br. J. exp. Path.*, **54**, 152–162.

YAMAMOTO, S., DUNN, C.J., CAPASSO, F., DEPORTER, D.A., & WILLOUGHBY, D.A. (1975). Quantitative studies on cell-mediated immunity in the pleural cavity of guinea-pigs. *J. Path.*, **117**, 65–73.

YAMAMOTO, S., DUNN, C.J., & WILLOUGHBY, D.A. (1976). Studies on delayed hypersensitivity pleural exudates in guinea pigs. I. Demonstration of substances in cell-free exudate which cause inhibition of mononuclear cell migration *in vitro*. *Immunology*, **30**, 505–511.

Modulation of spontaneous and acetylcholine-induced contractions of rat ileum by betamethasone

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Anti-inflammatory steroids inhibit the contraction of smooth muscle produced by various stimulating drugs (Bass & Setliff, 1960). Dexamethasone (10^{-5} g/ml and above) inhibits both the electrically-induced and acetylcholine-induced contractions of the guinea-pig ileum (Cheng & Araki, 1978). In this study the effects of betamethasone disodium phosphate (10^{-10} to 10^{-3} g/ml) on the contractions of the rat ileum are reported.

Male Sprague-Dawley rats (200 g) were killed and 2 cm pieces of ileum were dissected out into Krebs' solution. Contractions were recorded with a Statham isometric transducer and a Grass Polygraph.

Spontaneous contractions occurred when a piece of tissue was suspended in Krebs' solution at 37°C. The tissue was allowed to contract for a 10 min control period. The drug was added, left in contact for 10 min and washed out. After a 10 min recovery