

## The effects of a human plasma fraction on adjuvant arthritis and granuloma pellet reactions in the rat

A fraction prepared from normal human plasma has been shown to inhibit acute paw oedemas in the rat induced by either carrageenan (Ford-Hutchinson, Insley & others, 1973), dextran (Elliott, Ford-Hutchinson & Smith, 1974) or yeast (Bolam, Elliott & others, 1974). When injected intravenously the fraction (1 ml of the combined fractions II and IV, Ford-Hutchinson & others, 1973) has now been found to inhibit the development of the secondary lesions in adjuvant arthritis but not to affect the deposition of granulation tissue around implanted cotton wool pellets in the rat. The results in the adjuvant arthritis test for the development of all the secondary lesions are given in Table 1 and for the swelling of the contralateral uninjected hind paw in Fig. 1.

Table 1. *Effects of plasma fraction and indomethacin on development of secondary lesions in adjuvant arthritis test in the rat.*

Results given as means and expressed as total score for each group using an arbitrary scale of 0-3 for each lesion on uninjected paws, ears, nose and tail. The number of rats tested are given in brackets.

Group	Day after injection of adjuvant into right hind paw							
	11	12	13	14	15	16	17	18
Control (11)	1	2	3	6	7	10	12	15
Plasma fraction (10)	1	1	1	2	3	6	7	8
Indomethacin (9)	0	1	3	5	6	7	6	6

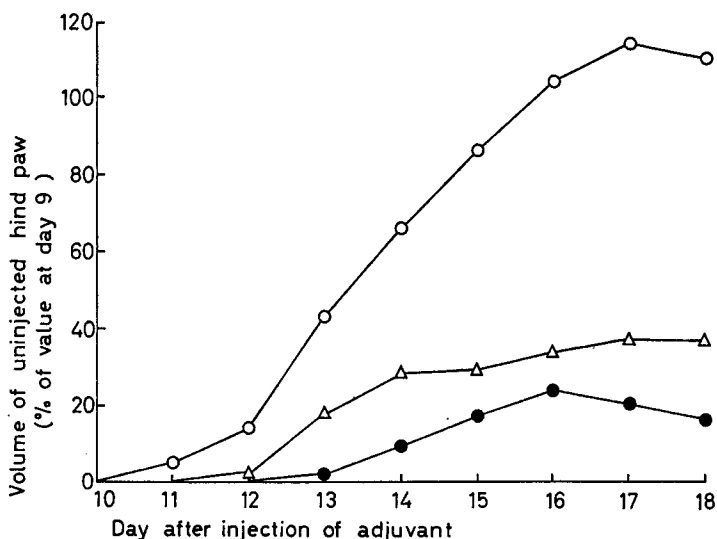


FIG. 1. Effects of plasma fraction and indomethacin on rat adjuvant-induced arthritis. Results calculated as volume of uninjected left hind paw as a percentage of value at day 9 after injection of the killed *Mycobacterium butyricum* in liquid paraffin into the right hind paw on Day 1. They are given as means for the following group; ○—○ saline control, 11 rats, ●—● plasma fraction, 10 rats, △—△ indomethacin, 9 rats. A statistically significant difference ( $P < 0.02$ ) between the saline-treated rats and those given either plasma fraction or indomethacin has been taken to represent a significant anti-inflammatory effect. Such an effect occurred with the group treated with the plasma fraction from days 12 to 18 and with indomethacin from days 15 to 18.

In each instance the daily administration of the plasma fraction from day 10 onwards delayed the development of the secondary lesions in the uninjected hind paw, the forepaws, ears, tail and nose and significantly inhibited the swelling of the uninjected hind paw from day 12 onwards. Indomethacin ( $2.5 \text{ mg kg}^{-1}$ ) was used as a reference drug and also produced a positive result. In contrast, the twice daily administration of 1 ml of the plasma fraction did not affect the formation of granulation tissue around implanted cotton wool pellets in the rat (Winter, Risley & Nuss, 1963) although the administration of indomethacin, in a daily dose of  $3 \text{ mg kg}^{-1}$ , significantly reduced the weight of granulation tissue around the implanted pellets compared to the values observed in control groups receiving injections of saline.

The human plasma fraction therefore not only exerts an anti-inflammatory effect in various acute paw oedemas but also inhibits the development of secondary lesions in the adjuvant arthritis test. The latter reaction not only reflects aspects of more chronic inflammatory processes but has been stated (Newbould, 1963) to be more akin to human rheumatoid arthritis than any other laboratory test. However, the fraction is not active in the cotton wool pellet reaction in the rat, another test in which the inflammatory stimulus is more sustained than in acute paw oedemas.

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