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The effect of dibutyryl cyclic amp on the chemotaxis and chemokinesis of rat polymorphonuclear leucocytes (pmn)

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PMN accumulation is an important aspect of the inflammatory response and its modification by drugs is therefore of interest with regard to the control of inflammation. Increased intracellular cyclic AMP levels have previously been associated with an inhibition of chemotaxis and we ourselves have observed such an inhibition using a microscopic technique of chemotaxis assessment (Bradshaw, Roch-Arveiller & Giroud, 1978). However, we have now tested the effect of dibutyryl cyclic AMP (db cyclic AMP) and cholera toxin on rat PMN migration towards casein using a filter method of migration assessment and in this case no inhibition was observed. Borel (1973) has previously also observed a lack of effect of both cyclic AMP and db cyclic AMP on the migration of rabbit peritoneal neutrophils, which appears to conflict with the results of Rivkin, Rosenblatt & Becker (1975) who used the same type of cells, though a different method of raising intracellular cyclic AMP levels. In the hope of providing a possible explanation for these differences we have studied the effect of db cyclic AMP on PMN migration towards various substances, since the use of different chemical stimuli represents a possible source of the conflicting results. Rat PMN were obtained from the pleural cavity four hours after the intrapleural injection of isologous serum. After washing the cells they were then incubated for 15 min at 37°C in either Hank's solution or db cyclic AMP (10^{-3} M). The cells were then incubated in Boyden chambers for 90 min at 37°C and assessment of their migration was performed using the leading front technique. The chemoattractants used included casein, the exudates derived from experimental pleurisies induced by the injection of either 1 ml of 1% calcium pyrophosphate or 0.1 ml of 1% carrageenan, supernatants resulting from the lysis of erythrocytes in hypotonic saline, and albumen. In order to distinguish between chemokinetic effects (effects on cell speed) and chemotactic effects (effects on cell direction) these substances were used in both the absence and presence of a concentration gradient.

As indicated above db cyclic AMP was without effect on cell migration towards casein. This compound similarly had no effect on cell migration towards a pyrophosphate exudate and had only a slight (stimulatory) effect on migration towards a carrageenan exudate. However a significant stimulatory effect was observed when erythrocyte lysates and albumen were used to stimulate cell migration. The effect of cyclic AMP on PMN migration was thus clearly dependent on the substance used to stimulate migration and this could be correlated with the chemokinetic and chemotactic effects operating in each case. Thus it was found that casein and the inflammatory exudates possessed both chemokinetic and chemotactic properties whereas the erythrocyte lysates and albumen possessed only chemokinetic properties.

Our results suggest therefore that db cyclic AMP is able to stimulate chemokinesis induced by other substances. Our previous results using a microscopic technique in which chemokinetic effects are not involved indicated that db cyclic AMP inhibits chemotaxis. Since the relative importance of chemokinetic and chemotactic effects will vary, depending on the technique used and the nature of the chemoattractant, the opposing effects of cyclic AMP on these two phenomena could well explain the varying effect of this compound on cell migration, observed both previously and in the present study. These results emphasise the need to distinguish between chemokinesis and chemotaxis when studying the effects of drugs on cell migration.

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