

we usually use penicillin, and the choice of drugs is really between penicillin and cloxacillin. When we are dealing with a septic arthritis, we usually think it is due to staphylococci. Is there any information you can give us about the protein binding of penicillin G?

DR. HOWELL Benzyl penicillin is much less highly bound than cloxacillin. Obviously it would diffuse into the joint very much better and would be the best drug to use against a penicillin-sensitive staphylococcus.

#### References

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#### Studies on the Mode of Action of Non-Steroid Anti-Inflammatory Drugs. By D. A. WILLOUGHBY and M. DI ROSA (St. Bartholomew's Hospital Medical College)

We have previously shown that analysis of the carrageenin-induced oedema in the rat paw is produced by a sequential release of mediators (Di Rosa, Giroud, and Willoughby, 1971). This model of inflammation is widely used in the screening of new anti-inflammatory agents—at the time when the inflammation is usually assessed (3 to 4 hrs) this coincides with the release of prostaglandins.

The methods employed for producing oedema in the rat paw and its assessment were as previously described by Di Rosa and Willoughby (1971).

It was found that the inflammatory response from 2½ to 6 hrs after the injection of carrageenin, *i.e.* the prostaglandin-mediated phase, is closely associated with the migration of leucocytes into the inflamed area. The following non-steroid anti-inflammatory drugs: aspirin, indomethacin, mefenamic acid, and butazolidin, all inhibit the migration of monocytes from the inflamed

vessels. These agents also inhibit the phagocytic activity of these mononuclear cells.

It is concluded that these agents exert their activity on the carrageenin model of inflammation by inhibiting the migration of monocytes, which in turn are responsible for prostaglandin release. The main effect of these agents is on the surface of the leucocytes inhibiting mobility.

#### Discussion

DR. B. VERNON-ROBERTS (London) With more tissue oedema, cells are generally separated more widely. How have you assessed the relationship between oedema and the cell counts in sections? This is always a difficult problem.

PROF. WILLOUGHBY We have not found this so difficult. We do a large number of cell counts per section.

PROF. C. A. KEELE (London) Do you think that the migration of monocytes is responsible for the prostaglandin release, or alternatively do the prostaglandins cause the migration of monocytes?

PROF. WILLOUGHBY I think the hidden meaning in your question, if I am not mistaken, is 'Are the cells carrying with them enzymes as Vane (1971) described for synthesizing prostaglandins, or alternatively, do we believe that they are carrying preformed prostaglandins?'. I think the latter is the way the relationship really exists. We believe that initially the leucocytes are responsible for the prostaglandin release, although it has been shown by Kaley and Weiner (1971) that prostaglandin E<sub>1</sub> is chemotactic for leucocytes using *in vitro* methods. Possibly other factors initiate the migration of cells and this is then maintained by prostaglandin E<sub>1</sub>.

#### References

- Di Rosa, M., Giroud, J. P., and Willoughby, D. A. (1971) *J. Path.* **104**, 15 (Studies of the mediators of the acute inflammatory response induced in rats in different sites by carrageenin and turpentine)  
 — and Willoughby, D. A. (1971) *J. Pharm. Pharmacol.*, **23**, 297 (Screens for anti-inflammatory drugs)  
 Kaley, G., and Weiner, R. (1971) *Nature (New Biology)*, **234**, 114 (Effect of prostaglandin E<sub>1</sub> on leucocyte migration)  
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