measured by radioimmunoassay using sheep anti-PGE₂-BSA. Drugs were added immediately before incubation using the following concentration ranges: indomethacin (0.1 ng—10.0 µg/ml); aspirin (1 ng—100 µg/ml); phenylbutazone (1 ng—100 µg/ml); feprazone (1 ng—100 µg/ml), and naproxen (1 ng—100 µg/ml); colchicine (1 ng—10 µg/ml); dexamethasone (1 ng—10 µg/ml); prednisolone (1 ng—10 µg/ml), and dehydrocortisone (1 ng—10 µg/ml).

Macrophages produce substantial amounts of PGE (mean 11.6, range 2.4—43.2 ng, PGE₂ equivalent/10⁶ cells/24 h) whereas neutrophils produce much less (mean 0.4, range 0.2—0.62 ng, PGE₂ equivalent/10⁶ cells/24 h) measured by radioimmunoassay. The production of E-type PG by macrophages is inhibited by NSAIDs with a rank order of potency, on a weight basis, of indomethacin > feprazone > aspirin > phenylbutazone > naproxen > sodium salicylate. Anti-inflammatory glucocorticosteroids also inhibited macrophage PGE synthesis with a relative potency of dexamethasone > prednisolone > hydrocortisone. Colchicine, however, stimulated PGE production by the macrophages.

Whereas human rheumatoid synovial fragments produce substantial amounts of PGs and show comparable susceptibility to anti-inflammatory drugs as exhibited by guinea pig peritoneal exudate macrophages, cells present in human synovial effusions (predominantly polymorphonuclear (PMN) leucocytes) are poor effective sources of PGs *in vitro*. It is noteworthy that there is no correlation between the levels of PG and the PMN leucocyte count in synovial effusions (Patrino *et al.*, 1975) and that the appearance of PGs in urate crystal induced synovitis precedes PMN leucocyte infiltration (Glatt *et al.*, 1974); also that human peripheral blood PMN leucocytes are poorly active in generating PGs (Zurier, 1975). Both the NSAIDs and the steroidal anti-inflammatory drugs showed an efficacy in blocking PG production which broadly paralleled their clinical effectiveness in the former case and closely followed the anti-inflammatory activity in the latter. The stimulation of PG production by colchicine has also been noted in human rheumatoid synovial cultures (Levine, 1973) and during urate crystal induced synovitis (Glatt *et al.*, 1974). These observations suggest that macrophages are the most likely source of PGs in inflammatory joint disease, and indicate that the guinea pig peritoneal exudate macrophage may be an appropriate model for the evaluation of anti-inflammatory drugs.

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Selective concentration and localization of gold in macrophages of synovial and other tissues during and after chrysotherapy in rheumatoid patients. B. Vernon-Roberts*, J. L. Doré*, J. D. Jessop†, and W. J. Henderson†. (*Bone and Joint Research Unit, The London Hospital**; *The University Hospital of Wales, Cardiff.†*) Published in full in the *Annals*, 1976, **35**, 477.

Changes in collagen of synovial membrane in rheumatoid disease. C. R. Lovell, M. I. V. Jayson, and A. J. Bailey (*Department of Medicine, University of Bristol, and Agricultural Research Council, Langford, Bristol*)

Gross thickening of the synovium is a principal characteristic of rheumatoid disease. However, knowledge of the structure of synovial collagen and the changes in disease is limited.

Rheumatoid synovia were obtained at surgery from 10 cases of age range 40–70 years. Control specimens, matched for age and site, were obtained from autopsies of patients who had no evidence of rheumatic disease. We analysed the synovial membrane for the genetic type of collagen and the nature of the intermolecular crosslinks by reduction with tritiated borohydride (Bailey *et al.*, 1970). The rates of collagen biosynthesis were determined from the formation of nondialysable ³H-hydroxyproline after incubation of the tissue in ³H-proline labelled culture media (Herbert *et al.*, 1974). Fractional precipitation of the pepsin-solubilized collagen as described by Chung and Miller (1974) showed the presence of polymorphic forms, and these were identified as type III (60%) and type I (40%) collagens in both normal and rheumatoid synovia.

Analysis for the presence of borohydride reducible crosslinks showed both dihydroxylysinoxidation and monohydroxylysinoxidation. A high proportion of the latter crosslink was present in young tissue, but failed to decrease during maturation. However, analysis of synovium from rheumatoid patients in the older age group showed the presence of a high proportion of dihydroxylysinoxidation, indicating increased collagen synthesis. In contrast to the crosslink found in scleroderma skin this crosslink is not cleaved by D-penicillamine and tissue culture studies indicate that D-penicillamine fails to inhibit the increased collagen synthesis of rheumatoid synovium.

In summary, the type of collagen proliferated in rheumatoid synovium appears to be similar to normal but possesses a more stable crosslink that is resistant to D-penicillamine. Furthermore D-penicillamine therapy does not inhibit the rate of formation of this new collagen.

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Friction and lubrication of artificial hip joints. A. Usworth (*Leeds*)

The lubrication of artificial hip joints has been recognized as being important for some time. Not only would any full fluid film lubrication help to reduce friction, but it would also reduce the wear rate of such prostheses. Experiments were done on different types of prostheses, namely metal on plastic and metal on metal, to determine