The influence of prednisolone (PRED) and methotrexate (MTX) on the cell and connective tissue content of subcutaneously implanted polyurethane sponges in rats. B. Vernon-Roberts, S. Hay, E. G. Cleary, O. W. Wiebkin, I. R. Garrett, P. M. Brooks, L. P. Bignold. Department of Pathology, University of Adelaide, South Australia 5000.

As part of a study of drug actions in chronic inflammation the effects of PRED and MTX on the histology and the content of collagen and proteoglycans of the inflammatory tissue in polyurethane sponges impregnated with heat killed *Mycobacterium tuberculosis* and implanted subcutaneously in hooded Wistar rats for up to 63 days were studied. Drugs were administered during the 6-day period prior to sponge removal 7, 21, 35, 49, and 63 days after implantation. The early phase (day 7) was characterised by a heavy neutrophil infiltrate, small amounts of collagen, and large amounts of proteoglycan: both drugs markedly suppressed cellular infiltration and also reduced the content of collagen and proteoglycan. The intermediate phase (day 21) was characterised by active granulation tissue, a marked increase in collagen, and the persistence of abundant proteoglycan. While neither drug had discernible effects on the cell or collagen content, proteoglycan was reduced by PRED treatment. The late phase (day 35 onwards) was characterised by the progressive maturation of granulation tissue, the appearance of granulomas and mononuclear infiltrates consistent with delayed-type hypersensitivity (DH), and a reduced content of collagen and proteoglycan. While both drugs markedly suppressed the histological features of DH and appeared to produce some suppression of proteoglycan content after day 49, no change was observed in collagen content.

The findings indicate that PRED and MTX have profound effects on the cellular events of acute and chronic inflammation, and influence the synthesis or degradation of connective tissue macromolecules at certain stages of the inflammatory process.