tion and emission spectra to those obtained with cephalexin (Barbhaiya & Turner, unpublished observations).

As cephalexin does not appear to undergo metabolism in man (Kirby, DeMaine & Serill, 1971; Brogard, Pinget & others, 1975) this fluorimetric assay may prove to be satisfactory for kinetic studies and routine estimations of the drug in human plasma.

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LETTERS TO THE EDITOR

Acute rheumatoid arthritis developing in a patient treated with salmon calcitonin: evidence against a major anti-inflammatory action of this hormone

N. J. Y. WOODHOUSE*, S. M. MOHAMEDALLY, F. SAEDNEJAD, *Department of Medicine, King's College Hospital Medical School, Denmark Hill, London, SE5 8RX, U.K.*

Calcitonin (CT) is known to reduce the increased vascular permeability produced by dextran in the rat paw. This anti-inflammatory action is independent of the fall in serum calcium and is inhibited by β-adrenergic blockade (Reisterer & Jaques, 1970). Salmon CT has also been shown to reduce carrageenan oedema and the severity of Freund's adjuvant arthritis in rats. Inhibition of prostaglandin release was postulated as a possible mechanism for these effects (Velo, De Bastiani & others, 1975). The same authors also reported clinical improvement in some patients with rheumatoid arthritis treated with salmon CT. These results suggest a possible therapeutic role for CT in certain inflammatory disorders. The present report, however, describes the development of acute rheumatoid arthritis in a patient whose Paget's disease was being successfully controlled by daily subcutaneous injections of salmon CT.

The patient, age 67 years, presented in 1973 complaining of pain in the left forearm and tibia which had been present since 1945. Deformity of the affected bones was first noticed in the mid-1950s and Paget's disease was diagnosed in 1958 by radiographs and bone biopsy. Progressive pain in the ankle joint and deformity of the tibia necessitated an arthrodesis in 1964 and a tibial oesteotomy in 1967. The tibia remained painful and she regularly consumed panadol and DF 118 (dihydrocodeine tartrate) tablets. Previous medication included butazolidine, sodium fluoride and mithramycin. Temporary relief of bone pain had occurred with the

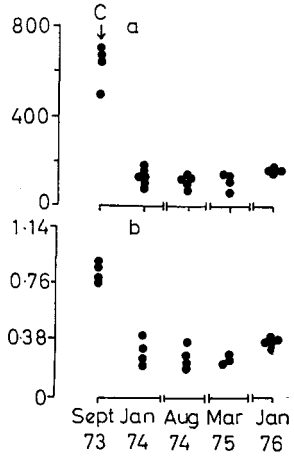

FIG. 1. Patient with active Paget's disease before and during therapy with salmon calcitonin. The individual a-serum alkaline phosphatase concentrations (IU litre^{-1}) are shown (normal range 30–85) and b-urinary total hydroxyproline concentrations (mM day^{-1}) (normal range 0·11–0·34). C-Control values.

* Correspondence.

mithramycin infusions which had been carried out the year previously. Apart from her bone pain the patient was in good health but with a strong family history of rheumatoid arthritis and thyroid disease. The patient had previously had a partial thyroidectomy for colloid goitre and a cholecystectomy.

A skeletal survey revealed Paget's disease confined to the left radius and tibia. The disease was active as judged by an elevated serum alkaline phosphatase and urinary hydroxyproline concentration as well as an increased uptake of radioactive strontium in the diseased bone. Because of the bone pain, treatment with synthetic salmon calcitonin (Calcynar) 50 MRCu (approx. 12·5 μg) twice daily subcutaneously, was instituted (Woodhouse, Reiner & others, 1971; Woodhouse, 1974). There was an immediate and sustained fall in urinary total hydroxyproline concentrations. Within a week the patient reported complete relief of bone pain and this, together with a biochemical remission of the disease, has been sustained on treatment for the last 116 weeks (Fig. 1).

In April, 1975, after 84 weeks on treatment, the patient noticed pains in the shoulders, elbows, wrists, knee and ankle joints. This was associated with weakness and lethargy, a reduced Hb of 11·7 g dl^{-1} an elevated ESR of 45 mm in the first hour and a positive rheumatoid factor at a dilution of 1/64. Straw coloured fluid was aspirated from an effusion in the right knee. No crystals were seen and the serum uric acid concentrations were normal at 0·28 mmol $litre^{-1}$. A diagnosis of rheumatoid arthritis was made and soluble aspirin was administered in addition to the calcitonin. Partial relief of the symptoms occurred. Throughout this period the patient's Paget's disease remained clinically and biochemically quiescent (Fig. 1). From our observations in this patient, it seems unlikely that CT exerts any significant prophylactic anti-inflammatory effect in rheumatoid arthritis. CT might, however, prevent the development of oesteoporosis that can occur in patients with rheumatoid arthritis.

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The binding of phenothiazines and related compounds to human serum albumin

J. H. PERRIN*, A. HULSHOFF, *Farmaceutisch Laboratorium, Rijksuniversiteit Utrecht, Catharijnesingel 60, Utrecht, The Netherlands*

In a recent publication (Sharples, 1976) it has been concluded from measurements of R_m values, binding constants and charge transfer complexation constants that the binding phenomenon following the interaction of albumin and a series of phenothiazines and imipramines is the result of predominantly electronic rather than hydrophobic interactions. We believe that problems arising from experimental design and interpretation cast serious doubts on the validity of these conclusions. The hydrophobicity of the molecules was determined by a reversed phase thin-layer chromatographic technique using liquid paraffin on a silica gel support and developing with a mixture of 9 parts acetone and 1 part water. In investigations (Mercier, 1968) using paraffin and methanol–water mixtures as the solvent system to determine R_m values by a reversed phase chromatographic technique, silica gel was found to be an unsatisfactory support phase for phenothiazines because of the strong adsorption of the drugs onto this support. Kieselguhr and cellulose were found to be more suitable. When partition coefficients or R_m values are to be correlated with binding constants for drug-albumin complexes it is preferable to make measurements using buffers or aqueous solutions containing as low a concentration as is possible of a water miscible organic solvent. (Tomlinson, 1975). We have measured the R_m values of a series of phenothiazines using oleyl alcohol, and aqueous methanol with Kieselguhr as a support phase (Hulshoff & Perrin, 1976). R_m values for the molecules were plotted as a function of methanol concentration to obtain the R_m^- value at zero methanol concentration. The lines for the various phenothiazines are not parallel and can cross at higher methanol concentrations. Similar observations using the apolar silicone oil and acetone–water mixtures for steroids (Biagi, Barbaro & others, 1975 a), penicillins (Biagi, Barbaro & others, 1969), phenols (Biagi, Gandolfi & others, 1975 b), as well as for phenothiazines (Guerra, Barbaro & Biagi, 1972) have been made, the lines frequently crossing at acetone concentrations of 60–70%. This means that at high co-solvent concentrations R_m values can be obtained which do not agree with expected hydrophobicities of the molecules under investigation. Sharples, using 90% acetone in his investigations, shows

* Correspondence.