Anniversary: 50 years of glucocorticoid treatment in rheumatoid arthritis

Philip Showalter Hench (Fig. 1) was awarded the only Nobel Prize in rheumatology for his work on glucocorticoids. The first patient he treated had rheumatoid arthritis (RA) and he administered Compound E (cortisone) on 21 September 1948 with almost miraculous effect [1]. The impact of this event has been captured [2] by dividing the history of rheumatology into ‘BC’ and ‘AC’ (before cortisol and after cortisol). The identification and use of glucocorticoid treatment can legitimately be seen as a major breakthrough in modern medicine. Since its discovery, cortisol and its equivalents have been shown to be life saving in a variety of diseases and conditions, including anaphylaxis, asthma, intracranial compression, systemic lupus erythematosus and vasculitis. However, even after half a century, the use and potential for misuse of glucocorticoids in RA remain the subject of vigorous debate [3–6].

The clues which set Hench to investigate the adrenal cortex were his own observations that pregnancy and jaundice ameliorate RA [7]. He hypothesized that in both conditions the improvement was caused by elevated corticosteroid levels, and this observation directed him to work with Kendall, Slocumb and Polley in trying to isolate compounds found in the adrenal cortex. It was supposed (and may yet, in a way, turn out to be the case [16]) that RA patients might have latent hypoadrenia, suggested by the clinical impression that RA patients were asthenic, weak, sometimes had low blood pressure and had low blood glucose levels. The results of the first treatment of the first patients were dramatic [1, 8, 9]. There is an original coloured file in which Hench and his colleagues documented the functional status of their first patients climbing stairs before and during treatment with Compound E. When the patients were switched to cholesterol treatment, serving as placebo, their functional status became worse [1]. This corresponded quite well with the theory that RA was a disease with adrenal insufficiency and did not cause concern. The new cortisone treatment of RA was applauded with great enthusiasm. Hench and Kendall (along with Reichstein from Switzerland) were honoured with the Nobel Prize only 2 yr later [8], in 1950. A few sceptical voices were raised. Russel Cecil’s was one of them: ‘... hypoadrenalism is not the answer to the rheumatoid arthritis problem … Hench and Kendall have only given us two more drugs to fumble with’ [9]. As time passed, it became more obvious that cortisone, and the derivatives subsequently developed, cause many side-effects when administered for long periods [3, 4, 10]. Although local and intra-articular use of glucocorticoids provide benefit for RA sufferers [11], systemic treatment was placed as ‘third line’ in the treatment pyramid, following unsuccessful treatment with specific anti-rheumatoid drugs [4]. In practice, however, glucocorticoids are widely used in RA [6]. This is so even though there are surprisingly few well-designed, controlled clin-
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choice for those with elderly-onset RA. Evidence for the erosion-preventing effect of low-dose glucocorticoid treatment in early RA is accumulating [20–22], and glucocorticoids are used for ‘bridging’ therapy in patients starting gold, methotrexate and other second-line drugs [3, 4]. New prednisolone derivatives are being investigated for beneficial effects with a better safety profile [23]. Other developments in glucocorticoid therapy will certainly follow, perhaps linking treatment more closely to the diurnal rhythm of the HPA axis [24, 25]. As Weiss has pointed out: ‘No agents currently available are as effective as corticosteroids in alleviating the symptoms of rheumatoid arthritis’ [4]. Glucocorticoid administration in one form or another is destined in its second half-century to find a better defined place in the treatment of RA.

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References


Fig. I. Professor Philip Showalter Hench, drawn by Dr J. M. H. Moll [26]. Reprinted with permission.