DEXAMETHASONE

F. DUDLEY HART, M.D., F.R.C.P.

Westminster Hospital, London, S.W.1

Dexamethasone is 16α-methyl-9α-fluoro-Δ¹-hydrocortisone. As with triamcinolone, the introduction of a new radical at the C16 position, in this case a methyl group, more than neutralizes the sodium-holding effect of the fluorine at C9. It differs from triamcinolone in having a methyl instead of a hydroxyl group at C16; this substitution enhances the anti-inflammatory, or glucocorticoid, effect very considerably. It was produced by the laboratories of Merck, Sharp & Dohme under the trade name of 'Decadron' and put on to the market some ten years after Merck's original cortisone. It is therefore the latest of the cortisone analogues to appear.

It is a particularly potent substance. The equivalent dose ratio compared with its predecessors, as judged by its effect on patients with rheumatoid arthritis, seems to be 25 mg. cortisone = 20 mg. hydrocortisone = 5 mg. prednisone or prednisolone = 4 mg. Triamcinolone = (approximately) 0.85 mg. dexamethasone. It is, therefore, much the most potent of the adrenocortical steroids available for use in rheumatoid arthritis, asthma, pemphigus, ulcerative colitis and all the other conditions previously treated by its predecessors. It is not to be preferred to cortisone or hydrocortisone in adrenal deficiency states, such as Addison's disease and after adrenalectomy, where the parent substances are still the drugs of preference.

Bunim and his colleagues (1958) found that dexamethasone had a longer half-life than hydrocortisone after intravenous injection into the same group of normal human subjects. The same group of workers demonstrated a potent suppression of pituitary corticotrophin secretion and found that in patients with rheumatoid arthritis, 1 to 2 mg. daily of dexamethasone reduced the concentration of hydrocortisone in the plasma to zero within 24 hours and also produced a considerable decrease in urinary excretion of corticoids and 17 ketosteroids and a marked diminution in circulating eosinophils. In normal subjects they found no depression of aldosterone activity. Both Bunim et al. (1958) and Slater et al. (1959) found a definite negative calcium balance on high dosage, Bunim and his colleagues using 6 to 10 mg. a day.

On the existing evidence there is no doubt but that dexamethasone is a highly potent substance and milligram for milligram has a much stronger adrenocortical suppressing effect than its predecessors. The fact that all these steroid substances suppress adrenocortical function even after only a few days administration is not yet sufficiently appreciated in practice, nor the fact that this suppression may last in some cases for several months. Dexamethasone is no exception to this rule, but is rather, weight for weight, the most potent of the available steroids in this respect, though in equivalent therapeutic doses its adrenal suppressing effect is probably much the same as its predecessors.

When dosage is scaled down to appropriate therapeutic levels the effect in the different disorders for which these steroids are used seems to be very similar and the unwanted effects identical. In rheumatoid arthritis using a dose ratio of 1:5: dexamethasone:prednisolone, Hart, Golding and Brown (1959) found no significant difference, 12 of 30 patients preferring dexamethasone, 12 prednisolone and six being indifferent. In all measurable respects—swelling, tenderness, grip, sedimentation rate, and by the patients own subjective criterion of pain and stiffness there was nothing to choose between the two treatment groups. This estimation was made on periods of two weeks to three months therapy, but continuation over longer periods has not altered the authors' opinion that while some few patients prefer dexamethasone and do better on it, the majority progress much as before and a few deteriorate on it and do better on other steroids. The fact that it is more potent is of no practical importance unless it can be shown that at lower dosage therapeutically effective levels side-effects are less common. Such does not appear to be the case. On the short term study quoted above Hart et al. (1959) found no difference in dyspeptic side-effects in the prednisolone and dexamethasone treated groups and Boland (1958) found that the
overall incidence of untoward effects was about the same as with prednisolone. He noted that the symptoms peculiar to triamcinolone—headache, dizziness, fatigue, anorexia, weight loss, muscle weakness and erythema—were not seen in his series of cases with dexamethasone, whereas increased appetite, weight gain and abdominal distention or “bloating” were. At the fourth European conference in Istanbul held in September 1959, several workers (West, Plotz, Villa) noted undue gain in weight and appearance of oedema in a number of cases. Robecchi (1959) for this reason now gives triamcinolone mixed in a tablet with dexamethasone in order to reduce this tendency to water loading. Both Plotz and Villa noted less interference with glucose metabolism than with other steroids and considered dexamethasone might have a place in treating diabetic patients where steroid therapy was required. Plotz found that none of ten diabetics treated on dexamethasone worsened, though one other patient, not known to be diabetic, developed glycosuria. Newman et al. (1959) however, found in three cases of diabetes mellitus a similar increase in fasting blood sugars and urinary glucose with both dexamethasone and hydrocortisone.

Reports on the treatment of other conditions are sparse. In our own experience there is little to choose between dexamethasone and prednisolone in systemic lupus erythematosus, asthma, and scleroderma. Stresemann (1959), in Berlin, found that in asthma dexamethasone was, weight for weight, five times as effective as prednisone, though in different cases it appeared to vary from three to eight times in efficacy. He found the ratio more variable than with triamcinolone and concluded that these two newer substances had little to offer over prednisone. Three cases developed oedema on dexamethasone which disappeared when transferred to prednisone.

In conclusion, it seems likely that though dexamethasone is the most potent of the adrenocortical steroids generally available this fact is of little importance when the dose is scaled down to the equivalent effective level unless it proves to have fewer side-effects or is cheaper than its predecessors. Neither is the case. Side effects appear to occur, as much as with prednisolone or prednisone. Oedema and gain in weight may occasionally be troublesome though usually readily controlled by oral diuretics. Evidence that it is less diabetogenic is suggestive but non-proven. It is a potent suppressor of adrenocortical function and will probably prove useful in this respect in helping to control some cases of metastatic malignant disease and adrogenital syndrome when the smaller amount of steroid given will interfere less with biochemical studies on urine and blood. More time is necessary to evaluate thoroughly the clinical effects of this potent newcomer, but to date it appears to be as useful as its predecessors but with few, if any, definite advantages over them.

Dexamethasone is marketed as ‘Decadron’ (Merck, Sharp & Dohme). ‘Millicorten’ (CIBA) and ‘Dexa-Cortisyl’ (Roussel). Packing and retail price exempt p.t. is: 30 tablets (0.5 mg.), 368.; 100, 1148.; 500, 5558.

REFERENCES

Stresemann, E. (1959), Ibid., ii, 257.
West, H. F. (1959), Ibid., p. 60.

NOTICE OF SPECIAL INTEREST TO SUBSCRIBERS:

‘WHY NOT HAVE YOUR COPIES OF THIS JOURNAL BOUND INTO YEARLY VOLUMES?’

You can have your twelve monthly issues fully bound in dark green pin head cloth, lettered in gilt on spine with name of journal, Volume Number and year, complete with index at front, for 22s. 6d. post free. A limited number of out of print journals are available to bind into volumes and make your library complete. Price on application giving details of issues required to complete back volumes.

THE FELLOWSHIP OF POSTGRADUATE MEDICINE
60 PORTLAND PLACE, LONDON, W.1

WHY NOT HAVE YOUR JOURNALS BOUND?
Dexamethasone

F. Dudley Hart

*Postgrad Med J* 1960 36: 26-27
doi: 10.1136/pgmj.36.411.26

Updated information and services can be found at:
http://pmj.bmj.com/content/36/411/26.citation

These include:

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/