

THE EFFECT OF CORTISONE AND ACTH
ON MIGRAINE

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Of the many drugs, hormones, regimes and alterations of human physiology which have been found to benefit migraine, pregnancy has been recognized as one which brings about a prolonged and beneficial change in a high percentage of cases. Figure I discloses that, in our series of 51 migrainous mothers, 40, or 79%, were partially or completely relieved of headache through a substantial period of their pregnancy; and that, of the total number of 86 pregnancies in these mothers, 67, or 78%, were accompanied by partial or complete relief.

EFFECT OF PREGNANCY ON MIGRAINE

TOTAL NO. OF MIGRAINOUS MOTHERS	51
NO. PARTIALLY or COMPLETELY RELIEVED	40 (79%)
NO. NOT RELIEVED	11 (21%)
TOTAL NO. OF PREGNANCIES	86
PREGNANCY WITH COMPLETE RELIEF	48 (56%)
PREGNANCY WITH PARTIAL RELIEF	19 (22%)
PREGNANCY WITH NO RELIEF	19 (22%)

FIGURE I

The degree and regularity of relief to migraine which is thus demonstrated to be brought about by pregnancy makes it seem worth while to study in detail the mechanism by which these results are achieved in the hope that some light may be shed on the fundamental mechanism of migraine itself. One might consider various effects of pregnancy as being responsible, viz: the improved

mood of the patient, the increased blood volume, or the hormonal alterations which take place in the pregnant state. Dr. Hench¹ found, in the course of his clinical observations on rheumatoid arthritis, that both pregnancy and jaundice had a favorable effect on that condition. He also noticed that migraine is similarly affected. These observations led him to the hypothesis, since proved to be true, that one of the adrenal steroid hormones might be influential in altering the course of rheumatoid arthritis, and he implied that the same might be true for migraine. It seems logical as a first step, therefore, in the investigation of the means by which pregnancy affects migraine, to experiment with cortisone and ACTH. This paper intends merely to show whether these compounds influence migraine or not. It by no means intends to suggest them as therapeutic agents.

The first studies in this direction consisted of an effort to determine whether cortisone or ACTH were effective in stopping an acute attack of headache. Four trials were made, as shown, in Figure II and only slight, transitory benefit, if any could be demonstrated. In all these experiments, the degree of severity of headache was expressed by the patient on a scale ranging from 0 to 10 plus. Although this is an entirely subjective response, it has been found that patients who experience headache frequently give reasonably consistent estimates of their head pain. At the time these acute experiments were performed, cortisone and ACTH were available only in small amounts, and it is possible that the failure to demonstrate significant relief was due to the use of an insufficient quantity of the hormones.

When cortisone became more available, it was decided to try a long-term experiment. The patient selected for this purpose was a 53-year-old woman who began having typical migraine attacks at the age of 11. The frequency of her headaches had gradually increased through the years until extremely severe, 10 plus, headaches had become a daily event for the past six months. Gynergen regularly relieved her attacks, but left her feeling sick and miserable

¹Hench, Philip S., *The Potential Reversibility of Rheumatoid Arthritis*. Proc. Staff Meetings of Mayo Clinic, Vol. 24, p. 167, March 30, 1949.

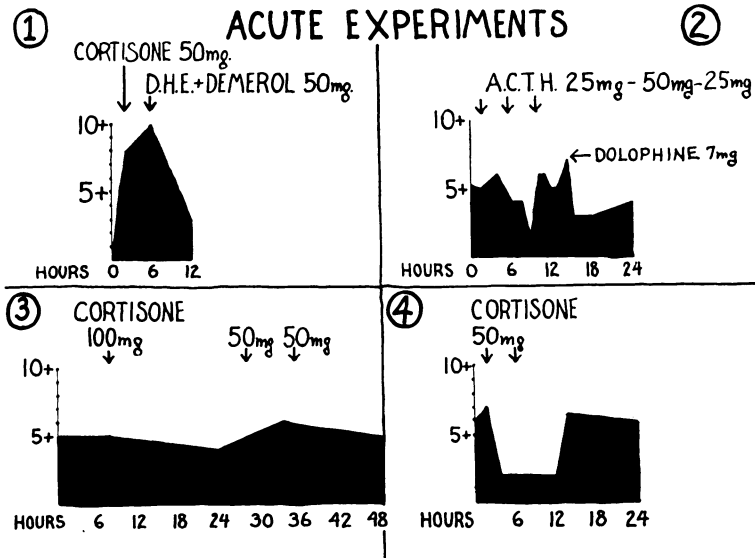


FIGURE II

for the rest of the day. In addition to her headaches, she suffered constantly from marked fatigue, nausea, dizziness, weakness and joint pains. She had mild, but definite changes in her mid-phalangeal joints consistent with rheumatoid arthritis. The only period of relief from headache which she had ever experienced, in spite of a multitude of treatments and hospitalizations, had been during her one pregnancy. Figure III demonstrates the effect of cortisone upon this patient's headache and other symptoms when she was brought into the hospital on June 15, 1950. One may observe from the chart that after three days of cortisone therapy both her headaches and associated symptoms were markedly alleviated. As the dosage of cortisone was tapered off to low levels, and finally stopped, the patient's headaches began to recur, soon to be followed by all her other distressing symptoms.

The next patient to receive cortisone therapy (see Figure IV) was a 33-year-old woman whose mother had had sick headaches and whose own headaches began within three months after the de-

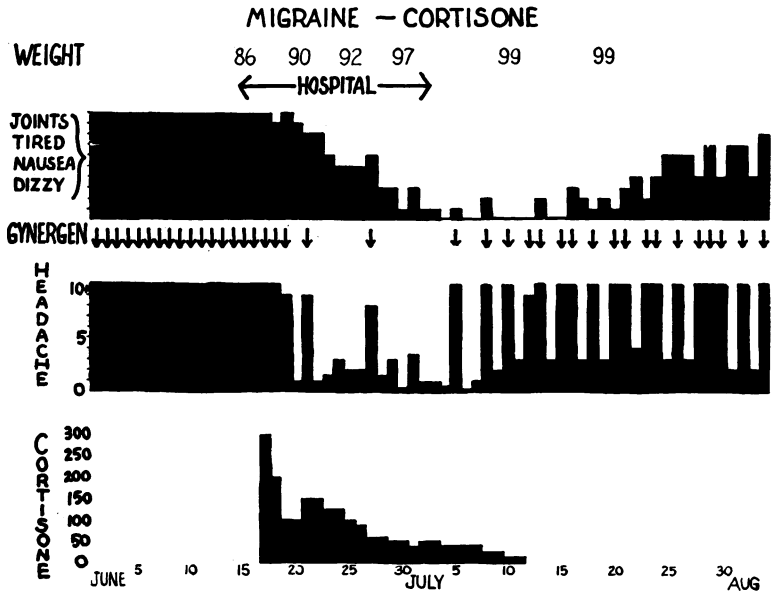


FIGURE III

livery of her first baby. At the beginning, they were associated only with her menstrual periods, but, before long, they began to come in between periods as well, and to last more and more days at a time. With her second pregnancy, she had headaches up to the third month when they disappeared completely until immediately after delivery. Many measures had been tried, with only transitory and inconsistent results for her relief. For several months, it seemed that testosterone, in some instances, prevented the development of an attack, or brought a headache which had already developed to an earlier conclusion. The effectiveness of this medication wore off, however, and the patient developed a headache which could not be relieved by any means, and continued steadily at an intensity of 5-10 plus daily for the six months preceding her entrance to the hospital for cortisone therapy. Three days after receiving cortisone, her headache abated to a negligible intensity, and ultimately disappeared entirely. She had one brief period of headache

MENSTRUAL MIGRAINE CORTISONE

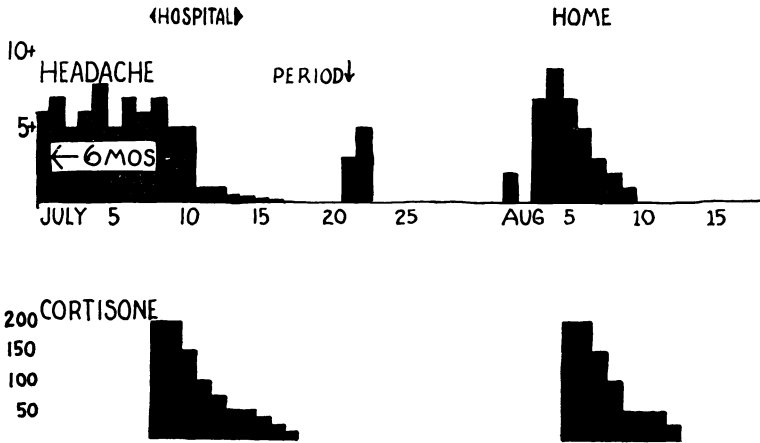


FIGURE IV

for two days, shortly after cortisone had been stopped, which cleared spontaneously. Two weeks later, she developed a very severe attack, which bid fair to develop into one of her prolonged and prostrating episodes. This was again brought under control in four days by cortisone. The patient has subsequently experienced no headache for the past two months.

The third patient was a 57-year-old woman with a life-long history of typical migraine, characteristically relieved by gynergen and associated with moderately severe aches in her joints and an irritable and depressed mood. This patient was at first given cortisone, and, although it greatly improved her joint symptoms (as demonstrated in Figure V) her headache was not much relieved, and her mood became so depressed that cortisone therapy had to be stopped. In reviewing this experiment, both patient and doctor noted that, although she continued to have plenty of headaches during cortisone treatment, the pain was in a different location,

data, to suggest that the response of her adrenal cortex was not adequate. Probably larger doses of ACTH should have been tried in order to make this experiment more conclusive.

The fourth patient was a woman 34 years old who had had attacks of left-sided head, neck and face pain, beginning at the age of 16. The pain came first intermittently in attacks, but finally settled into steady severe symptoms which had been present every day in some degree for the past six years. With the pain were associated marked symptoms of fatigue, and the patient had been forced to give up her job as a laboratory technician. She had become addicted to codeine. An operation severing the first and second cervical sensory roots had not relieved her symptoms. After a year of psychotherapy, she managed to get rid of her codeine, and to stand her constant pain more cheerfully. It still persisted, however, in severe degree, and was almost totally incapacitating.

ATYPICAL NEURALGIA — CORTISONE

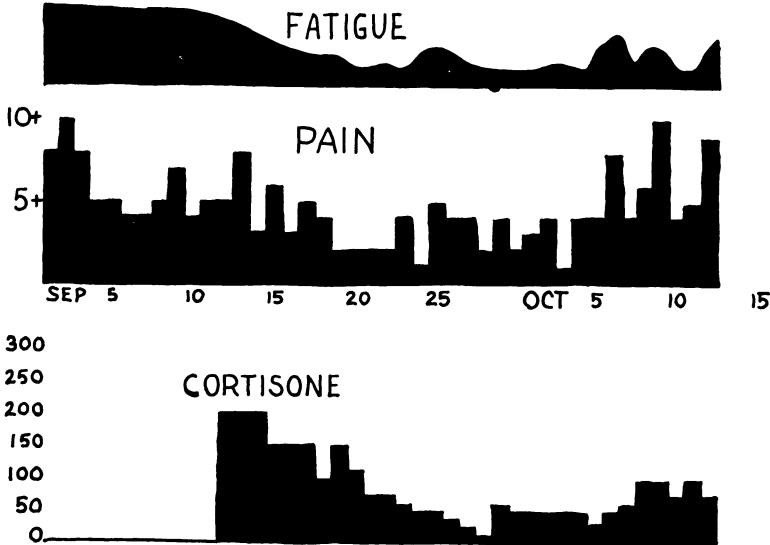


FIGURE VI

Upon being given cortisone, her fatigue and general malaise were so much relieved that she was able to resume her duties and her job. Her pain was relieved perhaps more than Figure VI would suggest, when one considers that she was carrying on normal activity during the period of cortisone therapy, and, in fact, had a tendency to overdo. It may also be said that the graph plots only the peak of pain which was achieved during each day, whereas, in the patient's experience, there were a great many more hours during each day in which she had relatively little pain, during the cortisone therapy, even though, at some point each day, usually at the end, she still experienced considerable suffering.

The last experiment was designed as a control. Since it could be argued that taking a patient out of a possibly stressful situation in her own home and placing her in a hospital, free from cares and the physical requirements of running a household, might in itself relieve migraine; and since it was thought possible that

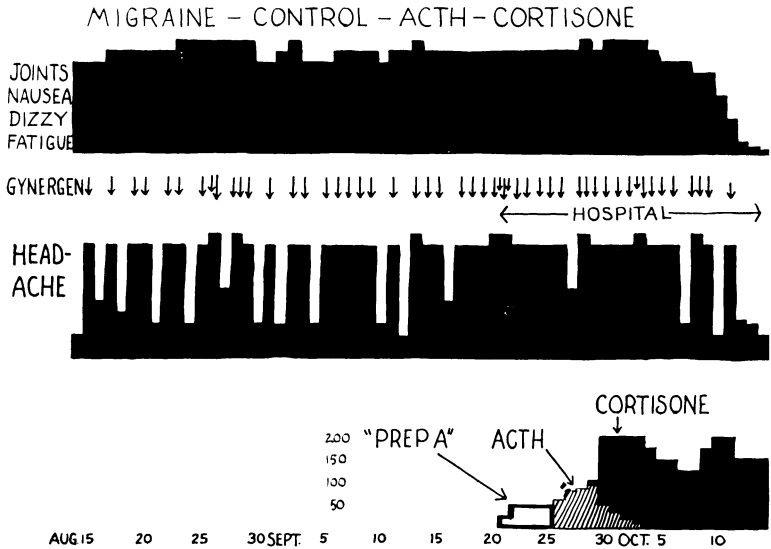


FIGURE VII

the psychological effect of receiving a new and much-acclaimed medicine might be powerful in relieving headache, it was decided to bring patient Number I back into the hospital for longer and more controlled observation. By this time, patient Number I had been off cortisone therapy for over two months, and it will be seen from Figure VII that her symptoms of headache had gradually returned to approximately the pre-cortisone level, and that the associated symptoms of joint pains, nausea, dizziness and fatigue had likewise reached their full intensity again. For the first five days of her hospital stay, she was given a cholesterol preparation, resembling cortisone in appearance, but devoid of physiological activity. She was then given ACTH over a total period of eight days, without any symptomatic response. It was felt, from her laboratory studies, that her adrenal cortex was not reacting well to the stimulation of ACTH, and so, on the fifth day of ACTH therapy, cortisone was added in full amounts, while the ACTH was tapered off. The response to cortisone on this occasion was later in occurring, and to date has not been as clear-cut as on the occasion when it was first tried. However, after six days of treatment, a break began to occur in the headaches, and the satellite symptoms improved considerably. By the end of eleven days of treatment, the weakness, nausea, dizziness and joint pains had entirely disappeared, the patient had a good appetite again, and a definite sense of wellbeing. For the first time in over two and a half months, she went for three days without a headache. It is at this point that the observations on this patient now stand.

SUMMARY AND CONCLUSIONS

1. A study of the histories of 51 migrainous mothers during 86 pregnancies reveals that 79% of the mothers achieved partial or complete relief of migraine; and that of 86 pregnancies, 67, or 78% were accompanied by partial or complete relief of headache.

2. The possible role of cortisone and ACTH in effecting this relief has been studied in four acute experiments, and five prolonged experiments.

3. In the doses used, cortisone and ACTH would not seem to be effective as a means for rapid relief of a migraine attack.

4. In the prolonged experiments, there is considerable evidence to suggest that cortisone and ACTH have a beneficial, if not entirely curative effect upon migraine.

5. These agents have a more strikingly beneficial effect upon the symptoms associated with migraine, such as weakness, fatigability, nausea, dizziness and joint aches.

6. The effect of these agents on older patients is transitory. In one younger patient, the benefit seems to have been prolonged for over two months.

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